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ARCHIVES OF SURGERY

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BILIARY INTESTINAL ANASTOMOSIS FOR OBSTRUCTIVE JAUNDICE

ANALYSIS OF ONE HUNDRED AND THIRTY-SEVEN CONSECUTIVE CASES *

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We have studied 137 consecutive cases in which anastomosis of the biliary and the gastro-intestinal tracts was carried out at the Mayo Clinic from 1919 to 1924 inclusive. We wished to ascertain, if possible, the end-results of these operations and any other related data which might be correlated and used in the interpretation of the clinical and pathologic manifestations of the various lesions. Obviously, in such a series there are many complications, great technical difficulties and a high mortality rate. The malignant cases were hopeless and the patients were usually in extremely poor general health when they presented themselves for treatment. Many of them were jaundiced and had had previous operations, some of which had caused their chief complaint, as for example, strictures. All were poor risks and required heroic measures for cure, or even for some degree of relief.

Every patient with jaundice, or who had recently been jaundiced, was observed in the hospital before operation. A diet high in carbohydrates was given, fluid was forced, and calcium chloride was administered intravenously. The coagulation and calcium time of the blood were estimated, the serum bilirubin was determined, and tests of hepatic function were carried out if indicated, as well as other special tests which might have direct bearing on the case. As soon as the serum bilirubin dropped to within normal limits and the patient's condition permitted it, operation was performed. In many cases, however, the serum bilirubin did not drop and surgical intervention was imperative, so the risk was accepted and the operation performed.

A review of results in individual cases was not encouraging, but by studying the series as a whole and noting the progress of the various groups, we found that the end-results were better than we had anticipated in cases in which there was even a reasonable chance of improvement or cure.

* From the Division of Surgery, Mayo Clinic.

For purposes of comparing malignant and benign lesions, the cases were divided into series: (1) carcinoma of the pancreas, thirty-four cases; (2) carcinoma of the ducts, nine cases; (3) carcinoma or pancreatitis, fourteen cases; (4) pancreatitis, eleven cases; (5) stenosis of the bile ducts, sixty-two cases; (6) intrahepatic jaundice (biliary cirrhosis), four cases, and (7) miscellaneous, three cases (one congenital absence of the common duct, one perforating duodenal ulcer causing obstruction of the duodenum and common duct, and one painless jaundice without demonstrable cause). For obvious reasons cases of the same series in which some condition is common to all will be compared.

TABLE 1.—*Carcinoma of Pancreas (First Series)*

			Age, Years			Duration of Symptoms			Duration of Jaundice			Type of Jaundice			Patients Surviving Operation		
	Patients	Percentage	Average	Oldest	Youngest	Average, Months	Longest, Years	Shortest, Months	Average, Months	Longest, Months	Shortest, Weeks	No Jaundice	Intermittent	Constant	Not Heard From	Heard From	Average Postoperative Life of Patients Now Dead, Months
Group 1: Colic alone	12	35.29	55.3	70	34	34.25	10	0.5	7.3	48	2	..	5	7	..	4*	9.7
Group 2: Pain alone	8	23.52	59.2	72	49	12.5	5	10	1.5	3	1	1	1	6	2	2†	9.5
Group 3: No colic or pain.....	13	38.23	59.9	81	42	3.5	0.83	0.5	1.5	3	2	..	..	13	2	5‡	4.6
Group 4: Both colic and pain...	1	2.94	67	..	..	60	..	....	0.75	..	..	..	..	1	..	1§	7

* Two lived six months, one nine months, and one eighteen months.
† One lived four months, and one fifteen months.
‡ One lived three months, one four months, two five months, and one six months.
§ Lived seven months.

CARCINOMA OF THE PANCREAS (FIRST SERIES)

This series of thirty-four cases is subdivided into four groups (table 1). In group 1 were twelve cases (35.29 per cent) in which colic without pain was the chief symptom as distinguished from pain with or without jaundice; in group 2, eight cases (23.52 per cent) in which there was pain without colic; in group 3, thirteen cases (38.25 per cent) in which there was neither pain nor colic, and in group 4, one case (2.94 per cent) in which there was both pain and colic. In the past it has been generally accepted that "painless" jaundice signifies a malignant condition. In this series of proved carcinoma of the pancreas, there was a history of pain, colic or both, in 61.75 per cent, while in only 38.25 per cent there was no pain or colic.

In the first group the symptoms had been present nearly three times as long as in the cases in which there was pain alone (second group), and ten times longer than in the group in which there was no pain or

colic (third group). In the first group the average duration of jaundice was seven and three-tenths months, and in the other two groups only one and five-tenths months. Intermittent jaundice was common in the first group in five of twelve cases, it was uncommon in the second group, and in the third, constant. The average length of life after operation in the first group was nine months, in the second group nine and five-tenths months, but in the third, only four and six-tenths months.

Life expectancy in the first group was definitely longer than in the other groups. It was shortest in the third group; in the second it was between the first and the third. This is interesting in view of Judd and Hallberg's report on the results of cholecystectomy in cases of cholecystitis graded 1 and 1—. They found that patients presenting histories of colic and pain alone were cured or improved more often by removing the gallbladder than were those whose predominating complaint was dyspepsia without pain or colic. Seventy-eight per cent of patients suffering from abdominal colic, and 91.2 per cent from typical biliary colic were either cured or greatly improved by removal of the gallbladder, and only 53.6 per cent with a history of dyspesia without colic or pain were cured or improved. These data are mentioned because of their apparent prognostic value. A stretch of the imagination may be required in order to compare cholecystitis to carcinoma of the pancreas; the comparison is made more for the purpose of calling attention to the relationship than for the purpose of drawing conclusions.

The history extending over many months which is elicited in certain cases of carcinoma of the pancreas may be interpreted as due to a lesion in the biliary tract, even though in most cases such a lesion is not found at the time of the operation; we are, instead, dealing with recent manifestations of what probably is an entirely new entity, the earlier symptoms possibly being due to an infective process in the biliary tract with periods of remission, a point strikingly brought out in cases of true pancreatitis. Possibly true pancreatitis exists before the malignant change, which would explain the relatively long duration of symptoms. It does not seem likely that carcinoma could have existed from the beginning of symptoms.

It will be noticed that age incidence and average life expectancy after operation are essentially the same in three groups, though slightly shorter in the group without pain or colic. The relation of the predominating symptoms, pain and colic, to the length of the history and the duration and type of the jaundice, is worthy of attention, but the end-results in all the groups are the same, as would be expected in cases proved to be malignant.

Jaundice, pruritus, purpura and hemorrhage make the life of these patients distressing, and although they cannot be cured something can be done, such as adequate drainage to relieve the intolerable symptoms. If there is biliary obstruction due to carcinoma of the pancreas, the most

logical procedure is some type of anastomosis between the biliary and gastro-intestinal tracts, thus providing long and adequate drainage and at the same time preserving the bile. The jaundice will disappear and the patient's last days will be spent in comparative comfort. This type of operation is, of course, wholly palliative, and yet occasionally in a case which appears to be carcinoma of the pancreas, cholecystogastrostomy or some such type of operation will result in cure. In such cases it must be assumed that the condition was chronic pancreatitis and not carcinoma. In certain cases it is extremely difficult to determine definitely whether the presenting lesion is carcinoma or pancreatitis, but the operative treatment is the same. Reference will be made to this again in the series, carcinoma or pancreatitis. Surgically, anastomosis is justifiable in all cases of carcinoma of the pancreas in which there is a reasonable chance that the patient may survive the operation. It prolongs the patient's life and relieves him of much suffering.

In this series, besides the original pancreatic lesion, biliary cirrhosis was marked in twelve cases (35.29 per cent), dilatation of the gallbladder in twenty-five (73.52 per cent), dilatation of the common duct in sixteen (47 per cent), enlarged regional lymph nodes in seven (20.5 per cent), hepatitis in one (2.9 per cent), ascites in four (11.7 per cent), metastasis to the liver in five (14.7 per cent), metastasis to the lungs in one, dilatation of the duodenum in one, extension of the process into the duodenum in one, duodenal ulcer in one, and postoperative biliary fistula in one. Gallstones were found in only one case; in one case gallstones had been removed from the biliary tract at a previous operation.

Operations had previously been performed on the biliary tract in five cases (14.7 per cent). The gallbladder had been drained in two cases one year and one month before, respectively, with only short periods of relief; stones were not found in either case. The gallbladder and common duct had been drained for stones in one case, with relief for two years, and in another, the gallbladder which did not contain stones had been removed, without improvement. In the fifth case the gallbladder had been anastomosed to the stomach three months previously, with relief for two months; recurring symptoms were due to contraction of the stoma. The anastomosis was reconstructed and the stoma enlarged.

Cholecystogastrostomy was performed in twenty-six of the thirty-four cases, cholecystoduodenostomy in four, cholecystojejunostomy in two, choledochoduodenostomy in one case and cholecystocolostomy in one. Much has been written concerning ascending infection by way of the stoma and lymphatics. Experimentally, infection or irritation is easily demonstrated in almost all cases in which the gallbladder is anastomosed to the intestinal tract. As would be expected, the infection is greatest when cholecystenterostomy or cholecystocolostomy is performed and much less when the anastomosis is with the duodenum or

stomach. Cholecystenterostomy or cholecystocolostomy is never performed save when it is impossible to utilize the stomach or duodenum, and in these cases the operation is for palliation and there can be no choice of method. It is expected that infection will result from direct extension or by the periductal lymphatics; this would not be likely to occur within the life expectancy period. The usual result of such infection probably is hepatitis and some degree of cholangitis, both of which are of secondary importance in the presence of carcinoma of the pancreas and other conditions which preclude the possibility of utilizing the stomach or duodenum in the anastomosis. In this series, there does not appear to have been a choice of operation. Obviously, high anastomosis should always be done if possible, regardless of the type of lesion.

One of the patients in this series who survived operation lived eighteen months; one, fifteen months; one, nine months; one, seven months; two, six months; one, five months; two, four months, and one, three months. Four were not heard from. We do not have any information concerning the details of one patient's life after he left the clinic. One of the remaining eleven patients had slight jaundice associated with mild attacks of dyspepsia, and three others had jaundice with pain and chills and fever coming on shortly before death. The remaining seven patients were free from jaundice, but four of these had had occasional attacks of dyspepsia with gas and bloating. All failed progressively. One patient died at home; necropsy confirmed our diagnosis of carcinoma of the pancreas.

Colic with jaundice occurred in 35.29 per cent of the cases, pain with jaundice in 23.52 per cent, and colic, pain and jaundice in 2.94 per cent. Thus colic or pain or both with jaundice occurred in 61.75 per cent and "painless" jaundice on only 38.23 per cent. The life expectancy after operation in cases in which there was pain or colic or both was twice as long as in those in which pain and colic were absent. The average postoperative life expectancy in all groups was seven and seven-tenths months. The relief from jaundice of patients surviving operation was complete and permanent in 63.63 per cent.

The types of anastomosis were not sufficiently varied so that conclusions could be drawn with regard to the type giving the best results, and the postoperative life of the patients was too short to make such evaluation.

CARCINOMA OF THE BILE DUCTS (SECOND SERIES)

The nine cases in this series (table 2) were grouped, as in the first series, with reference to the presenting symptoms. In general, the duration of the disease and the duration and type of the jaundice were similar to the first series. The series is divided into three groups. In group 1 were two cases (22.22 per cent) in which there was colic without pain;

in group 2, four cases (44.44 per cent) in which there was pain without colic, and in group 3, three cases (33.33 per cent) in which there was neither pain nor colic. In the first group the history was almost eight times longer; the type of jaundice was more varied but unlike that in the first series, the average duration of jaundice was approximately as short or shorter than in the second and third groups. In the second group the average duration of symptoms was shorter and the jaundice more often constant, while in the third group the average duration of symptoms was the shortest of all groups and the jaundice was always constant, while the average duration of jaundice was the longest of the three groups.

TABLE 2.—*Carcinoma of the Bile Ducts (Second Series)*

			Age, Years			Duration of Symptoms			Duration of Jaundice			Type of Jaundice		Patients Surviving Operation	
	Patients	Percentage	Average	Oldest	Youngest	Average, Months	Longest, Months	Shortest, Months	Average, Months	Longest, Months	Shortest, Months	Intermittent	Constant	Heard From	Average Postoperative Life of Patients Now Dead, Months
Group 1: Colic alone	2	22.22	47	51	34	60	60	60	2	3	1	1	1	2*	9
Group 2: Pain alone	4	44.44	53.5	61	44	7.7	24	0.75	1.2	3	0.75	1	3	2†	..
Group 3: No colic or pain.....	3	33.33	55.6	57	55	6	8	4	4.6	8	2	..	3	1‡	17

* One lived six months, and one twelve months.
† One was living five months and one twenty-one months later.
‡ Lived seventeen months.

The postoperative life expectancy in these three groups is a trifle longer than in the corresponding groups in the first series. Since there are only nine cases in this series, definite conclusions cannot be drawn, yet the similarity between the two series is close enough to warrant drawing attention to it.

In five of the nine cases the lesion was situated at the ampulla, in one it was low in the common duct, in two in the common duct just below the juncture of the cystic duct; the site of one was not specified. Biliary cirrhosis was present in four cases (44.44 per cent), dilated gallbladder in six (66.66 per cent), dilatation of the common duct in seven (77.77 per cent), ascites in two (22.22 per cent), and metastasis to the liver, enlarged glands, large spleen, and a perforated gallbladder, each in one instance. In only one case was there evidence of disease in the gallbladder, and in this the gallbladder had perforated.

Cholecystogastrostomy was performed in five cases, cholecystoduodenostomy in one case, choledochoduodenostomy in two cases and cholecystojejunostomy in one case.

The five patients who survived operation (three who had had cholecystogastrostomy, one cholecystojejunostomy, and one cholecystoduodenostomy) improved immediately and returned home with the jaundice cleared or clearing. One patient was much improved five months after the operation; he was however, having some dyspepsia and occasional chills and fever, but no jaundice. We have not heard from him during the last eighteen months. Three patients lived seventeen, twelve and six months, respectively. Two were permanently relieved of jaundice and one was completely relieved for a year, when there was recurrence of the former trouble and death occurred seventeen months after operation. In the remaining case, that of a man, aged 44, a history was elicited of typical textbook type of recurring gallstone attacks without jaundice. At operation dilatation of the gallbladder was graded 3, the dilatation of the common duct was graded 2, enlargement of the regional lymph nodes was graded 2, and chronic appendicitis was graded 2; the pancreas, stomach and duodenum appeared normal. Cholecystectomy and appendectomy were performed with relief of symptoms for two months, when constant painless jaundice appeared and lasted three weeks. A second operation was performed three months after the first. At this time dilatation of the common duct with white bile was graded 3, and enlargement of the regional lymph nodes was graded 2; the pancreas appeared normal. A tumor 2.5 by 0.5 cm. at the ampulla projected into the duodenum. Biopsy resulted in a diagnosis of colloid carcinoma. Resection of the ampulla of Vater and choledochoduodenostomy was carried out. The patient returned home with jaundice cleared and a gain of 75 pounds (34.9 Kg.) in weight. Eighteen months after the second operation, symptoms returned and a month later exploration, because of obstructive jaundice, revealed a firm mass involving the second portion of the duodenum. The evidence suggested probable involvement of the retroduodenal lymph nodes, doubtless recurrence of the carcinoma. The patient was now getting along fairly well (two months after the last operation and twenty-one months after the second operation), but complained of weakness. The jaundice had entirely disappeared.

Colic with jaundice occurred in 22.22 per cent of cases, pain with jaundice in 44.44 per cent, and "painless" jaundice in 33.33 per cent. The duration of symptoms was longer in the first group than in the other two groups. Unlike the corresponding groups in the first series, the duration of jaundice was longest in the group without pain or colic, but the type of jaundice was the same as in the corresponding groups in

the first series. The average life expectancy after operation was longer than in the first series; that is, twelve and two-tenths months, perhaps due to a lower grade of malignancy, or to the local structures which prevent rapid growth, extension or metastasis, or to all of these factors. Jaundice has been permanently relieved in 66.66 per cent of the cases. There is not a sufficient number of cases to draw any definite conclusion as to the comparative efficiency of the various types of operations.

CARCINOMA OF THE PANCREAS OR PANCREATITIS (THIRD SERIES)

In this series are fourteen cases in which it was impossible to determine at the time of operation whether pancreatitis or carcinoma of the

TABLE 3.—*Carcinoma of Pancreas or Pancreatitis (Third Series)*

			Age, Years			Duration of Symptoms			Duration of Jaundice			Type of Jaundice		Patients Surviving Operation		
	Patients	Percentage	Average	Oldest	Youngest	Average, Months	Longest, Years	Shortest, Months	Average, Months	Longest, Months	Shortest, Weeks	Intermittent	Constant	Not Heard From	Heard From	Average Postoperative Life of Patients Now Dead
Group 1:																
Colic alone	3	21.42	49	58	41	113.6	19	1	3	6	4	2	1	1	2*	2.25 yr.
Group 2:																
Pain alone	1	7.14	64	..	..	12	..	..	6	..	..	..	1	..	1†	
Group 3:																
No colic or pain.....	10	71.42	55.2	75	37	8.4	1.5	1.5	4.6	18	3	3	7	1	8‡	12.4 mo.

* One was living six years later and one lived two and a fourth years.
† Living six years later.
‡ One lived two months, one four months, two thirteen months, one twelve months and one thirty months; one was living twelve months and one forty-four months later.

pancreas was present. In group 1 were three cases (21.42 per cent) in which there was colic without pain; in group 2 was one case (7.14 per cent) in which there was pain without colic, and in group 3 were ten cases (71.42 per cent) in which there was no pain or colic. In many cases of chronic pancreatitis the pancreas is enlarged, hard, and nodular, grossly resembling carcinoma of the pancreas so closely that the conditions cannot be differentiated.

In the three groups in this series the relationship between the cases of colic alone, pain alone, and those of neither pain nor colic is more definite. The average duration of symptoms in the first group was one hundred thirteen and six-tenths months (table 3), in the second group (only one case) the duration of symptoms was twelve months, and in the third group the average duration was eight and four-tenths months.

Jaundice was constant in a third of the cases in the first group, constant in the one case in the second group and constant in seven and intermittent in three cases of the third group. This conforms to the corresponding groups in the first and second series. The duration of the jaundice was essentially the same in all the groups, but by comparing the duration of jaundice with the duration of symptoms in this series with the corresponding groups of the two previous series, it is seen that in the first group the duration was entirely out of proportion to the duration of symptoms. In other words, in the first group in the first series the duration of jaundice was comparatively long in relation to the duration of symptoms, while in the corresponding group in the second and third series, the duration of jaundice was extremely short when compared with the long history. Attention is directed to the fact that painless jaundice was present in a greater proportion of cases (71.42 per cent) than in the first two series (table 4).

TABLE 4.—*Symptoms (in Per Cent) in Various Series*

Series	Colic Alone	Pain Alone	No Colic or Pain	Pain and Colic
Carcinoma of pancreas	35.29	23.52	38.23	2.94
Carcinoma of ducts	22.22	44.44	33.33	.....
Carcinoma of pancreas or pancreatitis	21.42	7.14	71.42	.....
Pancreatitis	.....	.....	45.45	54.54

The associated lesions were similar to those in the first two series. Biliary cirrhosis was present in six cases (42.85 per cent), hepatitis in two (14.28 per cent), dilatation of the common duct in eight (57.14 per cent), dilatation of the gallbladder in twelve (85.71 per cent), enlarged nodes in three (21.42 per cent), large spleen in one case, ascites in one and gallstones in one.

In two cases appendectomy had been performed without improvement, and in one the gallbladder had been drained (no stones found) without improvement. In only one of the fourteen cases were stones found in the biliary tract.

Cholecystogastrostomy was performed in eleven cases, cholecystoduodenostomy in two, and choledochoduodenostomy in one case. One patient died in the hospital of pneumonia eight days after operation. Thirteen lived to go home. Two patients were not heard from. Two of the remaining eleven patients died from causes not related to the operation, one from nephritis thirty months afterward and one from an accident thirteen months afterward. They had all been completely relieved of symptoms. Five died thirty, twenty-seven, thirteen, four and two months, respectively, after operation; the average length of postoperative life was fifteen and two-tenths months. Four patients are alive, two six

years and one three years and eight months after operation; one patient, when last heard from one year after operation, had not had jaundice, chills or fever, but had had some dyspepsia and constipation. Three patients consider themselves cured, and one considers himself much improved.

One patient had had pain without colic for one year and constant jaundice for six months; an operative diagnosis of carcinoma of the pancreas, 95 per cent, and pancreatitis, 5 per cent, was made. After cholecystoduodenostomy was performed, the patient went home much improved. One year later he considered himself cured, and six years later he is well and living a normal life. This is an instance which exemplifies the value of operative treatment in these indefinite cases. Such a striking example of cure of an apparently hopeless condition emphasizes the desirability of rather heroic treatment. If the condition proves to be carcinoma, the patient has at least been relieved of jaundice and made fairly comfortable. If, however, the condition proves to be a benign lesion, great improvement or even cure may be expected.

In cases in which it is impossible definitely to differentiate carcinoma or an inflammatory process, anastomosis of the biliary tract to the intestine is a logical procedure. Such an operation may be considered an "operative, therapeutic test." If the patient is cured or improved and lives longer than the life expectancy for carcinoma of the pancreas, it may be assumed that the condition is pancreatitis, while if the patient survives the operation and dies within the life expectancy period, it may be assumed that the lesion was malignant and not pancreatitis. This may appear unscientific, but it is justified clinically by the results obtained. If the patient dies, apparently from carcinoma, the operation must be considered as palliative only. The average length of life after operation of patients who died was nineteen and six-tenths months.

The history-jaundice ratio in the first group of the third series is entirely unlike that in the first and second series.

PANCREATITIS (FOURTH SERIES)

There were eleven cases in this series. These cases cannot be separated according to the groups as in the three former series. In the first group were six cases in which there was a history of colic or pain, but the distinction was not clear and in the second were five cases in which there was neither pain nor colic (table 5).

In the first group the duration of symptoms averaged five and two-tenths years, in the second it averaged only ten and six-tenths months. The type and duration of jaundice in the two groups were the same, the intermittent jaundice being somewhat more common in the first group, similar to that in the corresponding groups of the previous three series.

The associated lesions were about the same in the two groups, but with the difference that the regional lymph nodes were greatly enlarged in three cases in the first group and in only one in the second group; the gallbladder was markedly dilated in four cases in the second group and in only one in the first group. Cirrhosis was specified in five cases (45.45 per cent), stone in the common duct in one case (9 per cent), dilated common duct in two cases (18.18 per cent), gallstones in one case (9 per cent), hepatitis in four cases (36.27 per cent), large spleen in two cases (18.18 per cent) and ascites in one case.

In two cases an operation had previously been performed on the biliary tract. In one case, cholecystostomy had been performed with seven months' relief, and in the other, cholecystostomy two years previ-

TABLE 5.—*Pancreatitis (Fourth Series)*

			Age, Years			Duration of Symptoms			Duration of Jaundice			Type of Jaundice		Patients Surviving Operation	
	Patients	Percentage	Average	Oldest	Youngest	Average, Months	Longest, Years	Shortest, Months	Average, Months	Longest, Years	Shortest, Months	Intermittent	Constant	Heard From	Average Postoperative Life of Patients Now Dead, Months
Group 1: With pain and colic....	6	54.54	37.5	55	20	62.4	28	0.75	10.3	1.25	0.75	4	2	6*	3
Group 2: No pain or colic.....	5	45.45	41.4	57	13	10.6	2	3	14.8	2	3	2	3	2†	9.5

* One was living two years later, one one year, one fourteen months, and one three years; one lived five years and one three months.
† One lived one and a third year and one three months.

ously had resulted in biliary fistula for one year. Cholecystoduodenostomy was then performed, with relief for one month. At the last operation the stoma was found to be completely closed and it was reconstructed over a tube.

Cholecystogastrostomy was performed in seven cases, cholecystoduodenostomy in three, and cholecystoduodenostomy and splenectomy in one case. All of the patients in the first group lived to go home. One died three months after operation, probably from carcinoma of the pancreas. The jaundice had been completely relieved. One patient died five years after operation from cerebral hemorrhage; he had been completely cured of his former trouble. Four others considered themselves cured three years, two years, one year and two months, and one year, respectively, after operation.

It is impossible to draw conclusive deductions from such a small series of cases. Yet, in the light of the three previous series, the prog-

nosis in the group presenting colic and pain is better than in that in which colic and pain were absent. The postoperative results in the first group were much better than in the second, which is entirely in keeping with the data in the corresponding groups of the first three series of cases.

There is a consistent prognostic relationship in the corresponding groups of all the series in regard to the cases presenting symptoms of colic or pain, as compared with those without pain or colic. In a large percentage of cases of a malignant condition in the pancreas or ducts and of carcinoma of the pancreas or pancreatitis there was jaundice with pain or colic, so that the "painless" type of jaundice cannot hold the same diagnostic importance as formerly, but the dilated gallbladder of Courvoisier's law can be accepted as a presumptive sign of carcinoma (table 6). In obstructive jaundice due to stenosis at the ampulla, inflammatory reactions of the pancreas, carcinoma, cicatrix and calculus must be considered. It is usually fairly easy to distinguish the latter, but in the other cases accurate differential diagnosis is often impossible. In the doubtful cases we have felt that exploration of the pancreas is not without danger, and on that account biopsy has been done in only a few cases. Doubtless biopsy is justifiable and is of great value if it can be done without adding to the great risk already accepted in performing an operation. Without biopsy, gross examination of the organ must be relied on. In carcinoma of the pancreas, the local reactions are usually less than in the inflammatory lesions, and the tumor is more easily felt as an extremely hard and indurated mass with adenopathy characteristically different from that in chronic inflammation. Too much significance cannot be placed on the presenting symptoms in making a differential diagnosis, because on analysis it will be found that in a high percentage of malignant cases the presenting symptoms will be colic and pain, as well as jaundice (table 4). The treatment in cases of obstructive jaundice consists in the relief of biliary retention, the treatment of the pancreatic lesion, and the treatment of the cause of the pancreatic lesion. The simplest operative technic which will warrant cure or relief from jaundice as a palliative measure is the best. Exploratory operation is sometimes necessary to establish a diagnosis. If carcinoma is present, a palliative operation is performed. If the condition is benign, jaundice should be relieved and some type of good biliary drainage instituted. In the benign conditions, from a pathologic point of view, cholecystostomy or cholecystectomy is the logical procedure, since it is believed that the original focus is in the gallbladder in a large percentage of cases. Removal of the gallbladder, however, does not relieve the patient from jaundice; thus a dangerous situation is brought about, for at some future time the gallbladder may be needed for an anastomosis to cause relief from jaundice. Cholecystostomy probably is the simplest opera-

tive treatment, but the drainage is not reliable; it is irregular and the fistulous tract may close too soon and cause a return of symptoms, or it may persist after the pancreatic lesion has been apparently cured. Also the bile is lost to the patient, which is serious in long-continued drainage. While the establishment of internal biliary fistula requires more operative procedures, it is probably desirable since long-continued drainage is secured and the bile is preserved for the patient's use, provided the anastomosis is not made with the colon. We have already mentioned the unexpected cure of an apparently hopeless condition by anastomosis of the biliary and intestinal tracts. In the doubtful case, in which a tentative diagnosis has been made, the internal biliary fistula is probably the best operative treatment, be it palliation for carcinoma, or a curative measure for pancreatitis.

In the cases in which cholecystogastrostomy has been performed for benign lesions, such as pancreatitis, the presence of bile in the stomach does not cause disturbance of digestion, as is commonly believed. Gastric

TABLE 6.—*Cases with Dilatation of the Gallbladder and Common Duct*

Series	Cases	With Dilatation of Gallbladder		With Dilatation of Common Duct	
		Cases	Percentage	Cases	Percentage
Carcinoma of pancreas	34	25	73.52	16	46
Carcinoma of ducts	9	6	66.66	7	77.77
Carcinoma of pancreas or pancreatitis	14	12	85.71	8	57.14
Pancreatitis	11	5	45.45	2	18.18

analyses following these operations consistently show bile in the gastric content and always some acid, combined and free, but in less than normal amounts. Anacidity which one might expect, is rarely found. Physiologically, from eight to ten times the twenty-four hour secretion of bile would be necessary to neutralize the secretion of the stomach for a like period, not taking into account the digestion of protein foods. In many instances, if an anastomosis has been made over a rubber tube the patient complains of "dyspepsia" until the tube has passed, and after this he is completely relieved of the digestive disturbance. A woman in whom hepaticoduodenostomy was made over a rubber tube had dyspepsia for twenty-two months. After the tube was passed, she was completely free from symptoms.

STENOSIS OF THE BILE DUCTS (FIFTH SERIES)

There were sixty-two cases of stenosis of the bile ducts in which a reconstruction operation was inadvisable or impossible because of the destruction or absence of the necessary structures. With one exception, operation had been performed previously on the biliary tract; in some cases multiple operations had been performed. The one exception was

that of a case in which there was a three-year history of recurring attacks of typical biliary colic, recently with questionable jaundice. The last attack was extremely acute and at the time of operation acute cholecystitis (graded 3) with stones was found. The common duct was densely adherent to the gallbladder, forming an extensive cicatricial stricture and an acute angulation of the duct. Dense adhesions were present in the regions of the gallbladder and duct. Any type of reconstruction operation would have been a failure, so the gallbladder was excised and hepaticoduodenostomy performed. The immediate results were good and six years after the operation the patient was living a normal life, with slight abdominal pain and jaundice at rare intervals, but the symptoms were not severe enough to cause him to consult a physician.

In five of the remaining sixty-one cases, cholecystostomy alone had been performed previously with an average of fifteen and six-tenths months' relief from symptoms. In twenty-seven, cholecystectomy had been performed with an average of two and four-tenths months' relief. There were twelve cases in which cholecystostomy and cholecystectomy had been performed at different times, with an average period of relief of symptoms after cholecystectomy of seven and three-tenths months. In four cases, in which the gallbladder had been removed and the common duct drained at the same time, the average period of relief was three and two-tenths months. In six cases in which cholecystectomy and drainage of the common duct had been performed at different times, the average period of relief after the last operation was two and six-tenths months. There were seven other cases in which there had been two or more operations at different times before the patients presented themselves at the Mayo Clinic (table 7). The primary operation was cholecystectomy in forty-three cases and cholecystostomy in eighteen.

It was noted that trouble appeared immediately after the primary operation in certain cases, while in others there was no evidence of trouble for some time afterward. In certain cases the stricture was probably the result of trauma at the time of the operation, while in other cases it was undoubtedly due to a continuation of the inflammation in the bile ducts, which finally resulted in obliteration. Many cases attributed to trauma are due to obliterative cholangitis. In thirteen cases persistent biliary fistula followed cholecystectomy; in one it followed cholecystostomy, and in five it followed drainage of the common duct. Persistent biliary fistula following cholecystectomy or drainage of the common duct is probably the direct result of injury to the duct at the time of the first operation, which emphasizes the responsibility a surgeon assumes in performing even simple cholecystostomy or cholecystectomy.

Pain and colic were common to all cases in this series. In only three was there no definite jaundice; in all the others intermittent jaundice of some degree was present. In those with biliary fistula, the pain, chills, fever and jaundice were the direct result of the inadequate drainage.

The various types of operations were hepaticoduodenostomy in forty-seven cases, hepaticogastrostomy in two, cholecystogastrostomy in one case, cholecystoduodenostomy in two cases, choledochoduodenostomy in seven, hepaticocholedochostomy in one case, and choledochohepaticoduodenostomy in two cases.

Eight patients died at home. The one who survived longest lived four and a half years after operation, apparently cured, then died from

TABLE 7.—*Stenosis of Bile Ducts (Fifth Series) Previous Operations; Sixty-One Cases (98.38 Per Cent)*

Patients	Previous Operations	Average Period of Relief From Symptoms After Last Operation, Months*	Longest Period of Relief, Months	Shortest Period of Relief, Months
5	Cholecystostomy	15.6	24	2
27	Cholecystectomy	2.4	9	None
12	Cholecystostomy and cholecystectomy	7.3	36	None
4	Cholecystectomy and choledochostomy at same time	3.2	6	1
	Multiple Operations at Different Times			
6	Cholecystectomy and choledochostomy	2.6	2	None
1	Cholecystostomy; cholecystectomy; choledochostomy	6	..	..
1	Cholecystectomy; second operation for "adhesions"	1	..	..
1	Cholecystectomy; operation for "adhesions"; hepaticoduodenostomy; reconstruction of stoma	2	..	..
1	Cholecystectomy; reconstruction of common duct	None	..	..
2	Choledochostomy; cholecystectomy; hepaticoduodenostomy	3.5	4	3
1	Choledochostomy; cholecystectomy; dilatation of stricture of common duct	None	..	..

* Average relief after last operation for all cases, four and seven-tenths months.

acute gastric obstruction which had required gastro-enterostomy. The patient who survived the shortest time lived ten months. In this case there had been a gradual return of symptoms, and death was due to "starvation." The average length of life of these eight patients was twenty-nine and six-tenths months. In all cases the immediate post-operative results had been good, with recurrence of symptoms and gradual failure. Three of the eight patients were jaundiced shortly before death, and two were mildly jaundiced at intervals after the operation.

Seventeen patients consider themselves cured at periods of from one to five years after operation, the average being one and seven-tenths years. Sixteen patients were greatly improved at periods ranging from two to six years after operation, the average being four years. They complain of infrequent mild attacks of abdominal pain without jaun-

dice; mild dyspepsia was mentioned occasionally. They are living normal lives, and working; they do not require the services of a physician. Nine patients are in fair health only. This means that they have more attacks of abdominal pain with or without jaundice. Two patients have had occasional attacks of pain, chills, fever and jaundice, but little dyspepsia. They are, however, living fairly comfortably, with one exception, a man, aged 61. Two patients (4.8 per cent) have not been heard from.

INTRAHEPATIC JAUNDICE (SIXTH SERIES)

In the four cases of biliary cirrhosis in this series, cholecystogastrostomy had been performed. The average history was of ten months' duration. Jaundice was constant and the average duration was nine and seven-tenths months. In each instance, besides definite and marked cirrhosis, the regional lymph nodes were markedly enlarged. An operation had been performed previously on only one case. The gallbladder had been drained and stones removed fourteen years before, with complete relief until one month before the patient presented herself for treatment. The immediate results were good, and one and a half years after operation she was much improved, but occasionally experienced slight jaundice and mild dyspeptic attacks in which "gas" was a prominent symptom. The three remaining patients have not been heard from.

MISCELLANEOUS (SEVENTH SERIES)

There were three cases in this series: congenital absence of the common duct; obstruction of the common duct and duodenum due to perforated duodenal ulcer, and jaundice from undetermined cause.

The first case was that of a baby girl, aged 5 months, who had been jaundiced since birth. There was general adenopathy and the liver and spleen were much enlarged. At operation the gallbladder was found buried in the liver and the common duct extended only to the gallbladder. There was a moderate amount of free bile-stained fluid in the abdomen and the liver and spleen were large. The side of the gallbladder and the common duct were anastomosed to the duodenum. The child died three days after the operation. At necropsy no connection was found between the bile ducts and the duodenum. The duct ended as a blind pouch; it was this pouch which had been anastomosed to the duodenum. There was cirrhosis of the liver, graded 1, and hypertrophy of the spleen. The cause of death was peritonitis and pneumonia.

In the second case, that of a woman, aged 49, there had been typical recurring attacks of biliary colic with nausea and vomiting, but without jaundice for six years. Two years previously the gallbladder had been drained, with relief for six months. Then a biliary fistula developed,

with return of the former symptoms. At operation, a large perforating duodenal ulcer was found which had caused marked deformity with obstruction of the duodenum and the common duct. The gallbladder was small and showed evidence of chronic cholecystitis. The stomach was moderately dilated. The biliary fistula was excised, and cholecystoduodenostomy and posterior gastro-enterostomy were performed. The patient recovered uneventfully and six years after the operation considered herself completely cured.

In the third case, that of a man, aged 62, indefinite dyspepsia had existed for four years, and six weeks prior to examination painless jaundice with nausea and vomiting had developed. At the time of operation the dilatation of the common duct was graded 2; stones could not be found. Enlargement of the regional lymph nodes was graded 2. The pancreas and ampulla were normal and the liver was in good condition. No cause could be found for the jaundice and a diagnosis of "jaundice of undetermined origin" was made. Cholecystogastrostomy was performed. The patient recovered uneventfully and left the clinic with the jaundice practically cleared. He returned eight months later with a small ventral hernia, of no consequence, and reported marked improvement. He had not been jaundiced since the operation. Occasionally he had been troubled with slight dyspepsia.

SUMMARY OF POSTOPERATIVE RESULTS

In the 137 cases discussed, there were nine of contraction of the stoma. Partial or complete contraction of the stoma occurred in seven of the forty-seven cases in which hepaticoduodenostomy had been performed for stricture. Return of symptoms occurred from one to six months after operation, the average being four and two-tenths months. Reconstruction of the stoma over a rubber tube was carried out in each instance. One patient was apparently cured and died from acute gastric obstruction one and a half years after operation. Five patients are still living from two to four and a half years after operation, the average being two and nine-tenths years. Two of the five have been completely relieved of their former trouble for four and a half and three years, respectively. Three are much improved, but occasionally have slight attacks of pain, chills, fever and jaundice, although not severe enough to require the services of a physician. There were two other cases in which the stoma of the anastomosis contracted and produced obstruction to drainage of bile. In one, cholecystogastrostomy had been performed for obstructive jaundice due to carcinoma of the pancreas. After two months there was a return of symptoms, requiring reconstruction of the contracted stoma. In the other case cholecystoduodenostomy had been performed for obstructive jaundice caused by pancreatitis. Return of symptoms necessitated enlargement of the contracted stoma.

BLOOD IN THE CEREBROSPINAL FLUID

RESULTANT FUNCTIONAL AND ORGANIC ALTERATIONS IN THE CENTRAL NERVOUS SYSTEM *

A. EXPERIMENTAL DATA

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This work has been done with the hope of experimentally producing lesions simulating those occurring in human beings when a small amount of blood escapes into the subarachnoid space.

METHODS AND MATERIAL

Eighteen adult dogs (exact age unknown) and twenty-six puppies (five litters), all less than 10 days old, were injected with whole blood. An average pup from each litter was used as a control.

The whole blood was obtained from the vein in the leg of the adult dogs and from the longitudinal sinus of the pups. Free mixture of the blood and cerebrospinal fluid was desired, and the blood was slowly injected into the cisterna magna, into the subarachnoid space over the cerebral hemisphere and in a few instances, into the cerebral ventricles.

The work was started on adult dogs with frequent injections of from 0.5 to 2.5 cc. of blood. Larger amounts could not be injected into the cisterna magna without causing serious respiratory symptoms, but in a few instances, as much as 5 cc. was tolerated over the cerebral cortex. In the beginning, when adult dogs were being used, it was thought that repeated injections at short intervals would be required to produce a disturbance comparable to that observed in human beings with bloody cerebral spinal fluid; for this reason, some of the earlier dogs received as many as six injections. In the later experiments with young pups, it was found that a single injection would sometimes produce symptoms; therefore, most of these pups received only one or two injections.

Ether anesthesia was used in the adult dogs. Morphine, 1/6 grain (0.01 Gm.) was given hypodermically about a half an hour before the administration of ether. Chloroform without morphine was used in anesthetizing the pups.

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* From the Neurological Laboratory of the Henry Phipps Psychiatric Clinic, Johns Hopkins University, with the assistance of the Epilepsy Medical Research Fund.

When the animals died or were killed, autopsies were performed. To avoid possible injury of the meninges in the removal of the brain, the skull containing the brain was sectioned with a fine saw and then immersed in 10 per cent formaldehyde. By this method any portion desired for photography or microscopic study could be exposed in the fresh state and the entire brain easily brought into contact with the fixing fluid. The tissue was embedded in paraffin unless the dura was included in the blocks, in which case celloidin was used. Hematoxylin and eosin stain was used.

CLINICAL COURSE

Immediately after the injection, the adult animals were restless, spastic and recovered from the narcosis slowly. At times the spastic extremities were active; in some cases, the movements simulated running. At other times, there were atypical convulsive seizures with frothing at the mouth. The day following the injections the animals were usually dull, but walked about the cage and took food. After the injections, the dogs were kept under observation in the laboratory from one to three hours; then they were returned to the animal room. Daily visits were made to the animals, and every few days they were brought into the laboratory and allowed to play about under observation from one to three hours. In this way, it was possible to record symptoms which varied from difference in behavior to severe convulsive seizures.

The clinical course in most of the adult dogs was short because of the brief intervals between the injections. Many of them died within a few days after the last injection with gradually increasing debility marked chiefly by emaciation and irritability. They were hypersensitive and would cry out if handled. One of the adult dogs was given four injections into the cisterna magna over a period of one month, and was kept under observation thirty days after the last injection. During this period, there was gradually increasing weakness; because of the poor physical condition, the dog was killed with chloroform. A section from the base (fig. 3) shows chronic checking.

The most striking clinical course was seen in the younger dogs. This was first noticed in the behavior of the animals that had received injections as compared with the controls. After recovery from the immediate effects of the injection, the pups were less active, so that the puppies that had been treated could be picked out of the litter by the fact that they retired to a corner of the room and showed little of the characteristic tendencies of such animals to play. When stirred to activity, they would lose interest much more quickly than the controls.

In spite of the fact that the puppies ate well, they were generally smaller and markedly thinner. The difference in size between the control animals and animals that had received injections was seen in a

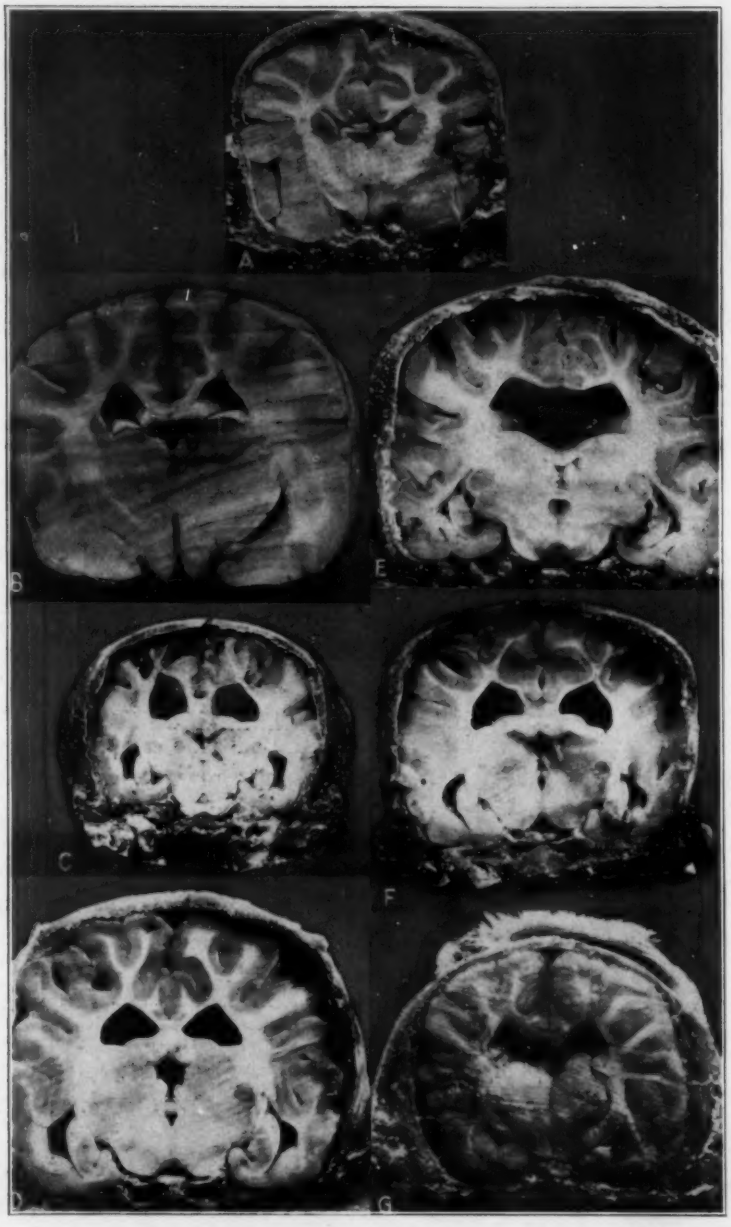

Fig. 1.—*A* indicates the frontal section through the brain of one of the control pups showing the normal ventricle to be very small; *B*, the dilated ventricle of adult dog 10 which received six injections of blood in the cisterna magna over a period of thirty-nine days and was killed two days after the last injection; *C*, the brain of pup 35 which received three injections of blood over the right cortex and two in the cisterna magna over a period of forty-two days and was killed twenty-one days after the last injection; *D*, the brain of pup 37 which received two injections of blood over the right cortex and two in the cisterna magna over a period of forty-two days and was killed seven days after the last injection; *E*, the brain of pup 45 which received one injection of blood in the cisterna magna and was killed twenty-one days later; *F*, the brain of pup 47 which received two injections in the cisterna magna over a period of seven days and was killed ten days after the last injection; *G*, the brain of pup 70 which received 1.25 cc. of blood in the cisterna magna and died sixty-two days later.

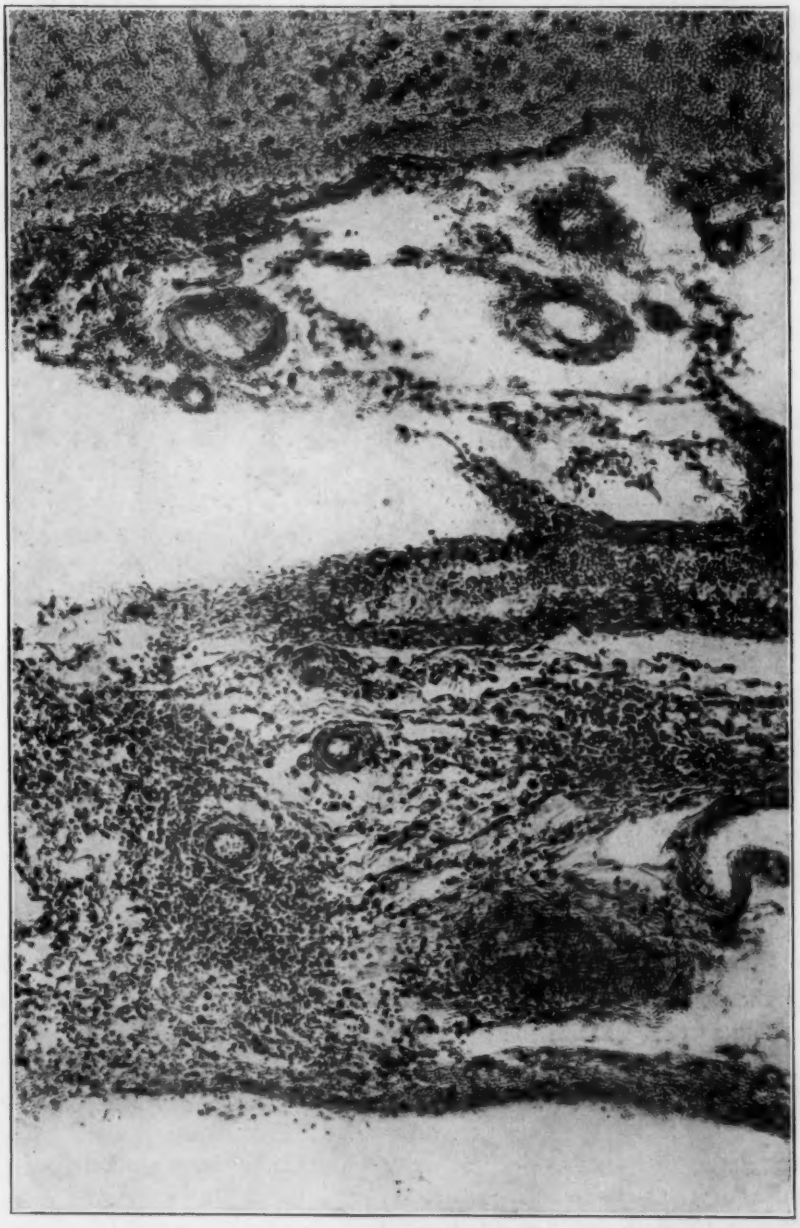

Fig. 2.—A section taken from the base of an adult dog which received four injections of blood from 1 to 1.5 cc. in amount into the cisterna magna over a period of seventeen days. The animal was killed two days after the last injection. The meninges were thickened and the seat of active cell proliferation.

pup (35, table 4) that had had five injections, three over the cerebral cortex and two at the base over a period of forty-two days. The first injection was given when the dog was 10 days old. When killed sixty-three days after the first and twenty-one days after the last injection, the general condition was fair. All the organs were normal except the brain. The dilatation of the ventricles was definite when compared with that of the control pup. Examination of the meninges showed chronic thickening over the base and cortex similar to that shown in figure 11. Another striking example was seen in a pup (54, table 1) which when 3 months old weighed scarcely half as much as the control. This pup had general convulsive seizures almost two months after the

TABLE 1.—*Protocols of Pups in Which Convulsions Occurred*

Date	Amount Injected	Remarks	Lesions
Pup 46			
April 23, 1926	1 cc. in cisterna magna	Satisfactory recovery	Meningeal thickening more marked over cerebral cortex where there is some scarring
June 7	.....	Severe general convulsions	
June 9	.....	Died	
Pup 50			
April 26, 1926	1 cc. in ventricle	Recovery	Meningeal thickening over cortex, chiefly at sulci; none over base
May 14	3.5 cc. over left cortex	Recovery	
May 17	2.5 cc. over right cortex	Recovery	
June 9	.....	Severe convulsive seizures; died	
Pup 54			
Jan. 21, 1927	0.5 cc. in cisterna magna	Respiratory embarrassment	Meningeal thickening at base and some areas of the cortex with cortical scarring
Feb. 11	0.8 cc. in cisterna magna	Very limp for some minutes following injection	
May 2	.....	Severe general convulsive seizures	
July 13	.....	Series of general convulsive seizures; died	
Pup 56			
Feb. 2, 1927	0.5 cc. in cisterna magna	Rapid recovery	Brain not sectioned; in poor condition when received in the laboratory
Feb. 4	1 cc. in cisterna magna	Rapid recovery	
May 18	.....	General convulsive seizure	
May 19	.....	General convulsive seizure	
Aug. 15	.....	Died	

last injection. Scattered areas of meningeal thickening were found during the examination of the brain, and there were areas of cortical scarring associated with the thickening (fig. 13).

Convulsive seizures immediately followed the injection in five of the ten adult dogs in which the blood was injected over the cerebral cortex, and in one of the four dogs in which blood was injected into the lateral ventricles. Convulsions did not occur immediately following the injections when young pups were used.

Four of the twenty-six puppies that received injections had convulsions after complete recovery from the immediate effects of the injection without indication of the seizure until a few minutes before the attack. The first pup (46, table 1) had a convulsion twenty-three days after the last injection; he survived for thirty-six hours, during which time there were a great many seizures. The second pup (50,

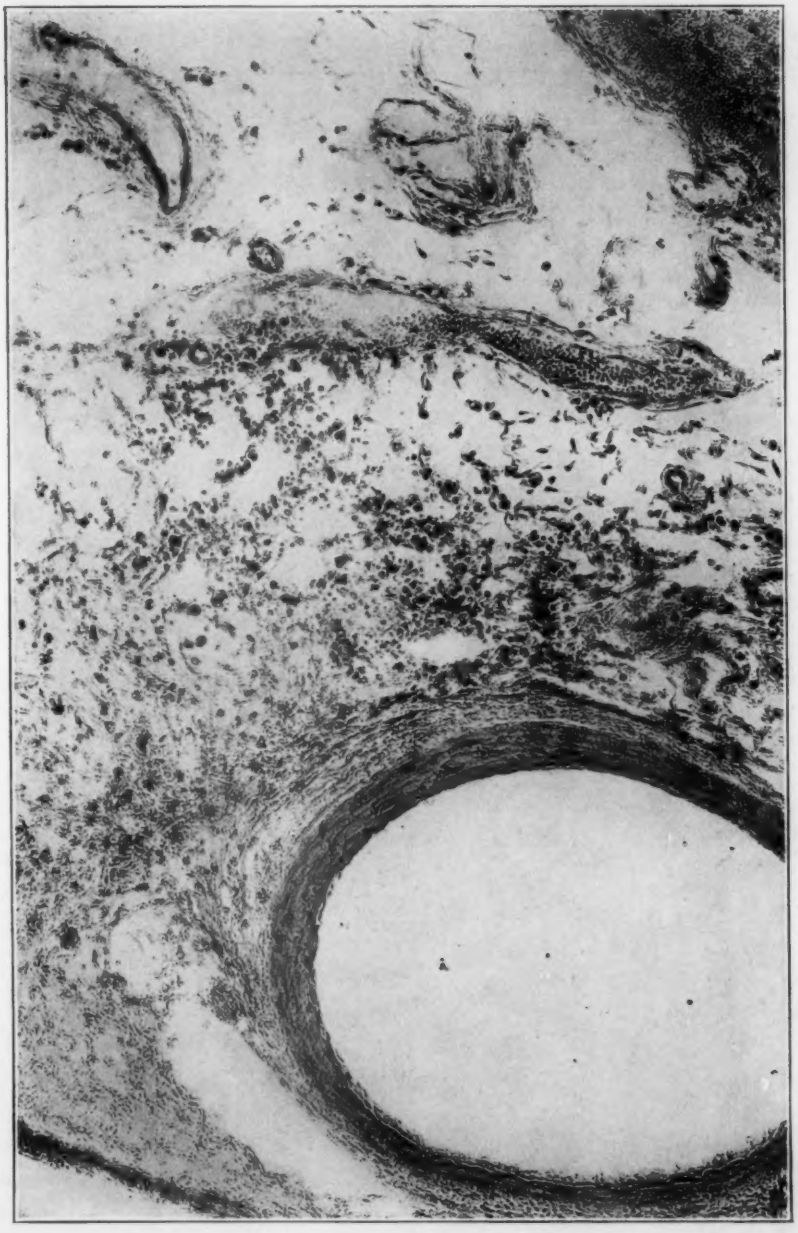

Fig. 3.—A section taken from the base of an adult dog which had four injections into the cisterna magna over a period of thirty-one days; the animal was killed thirty days after the last injection. In comparison with figure 2, there is a diminution of cells, but an increase of fibrous tissue. The fibrous tissue mesh contains a number of pigment-loaded phagocytes.

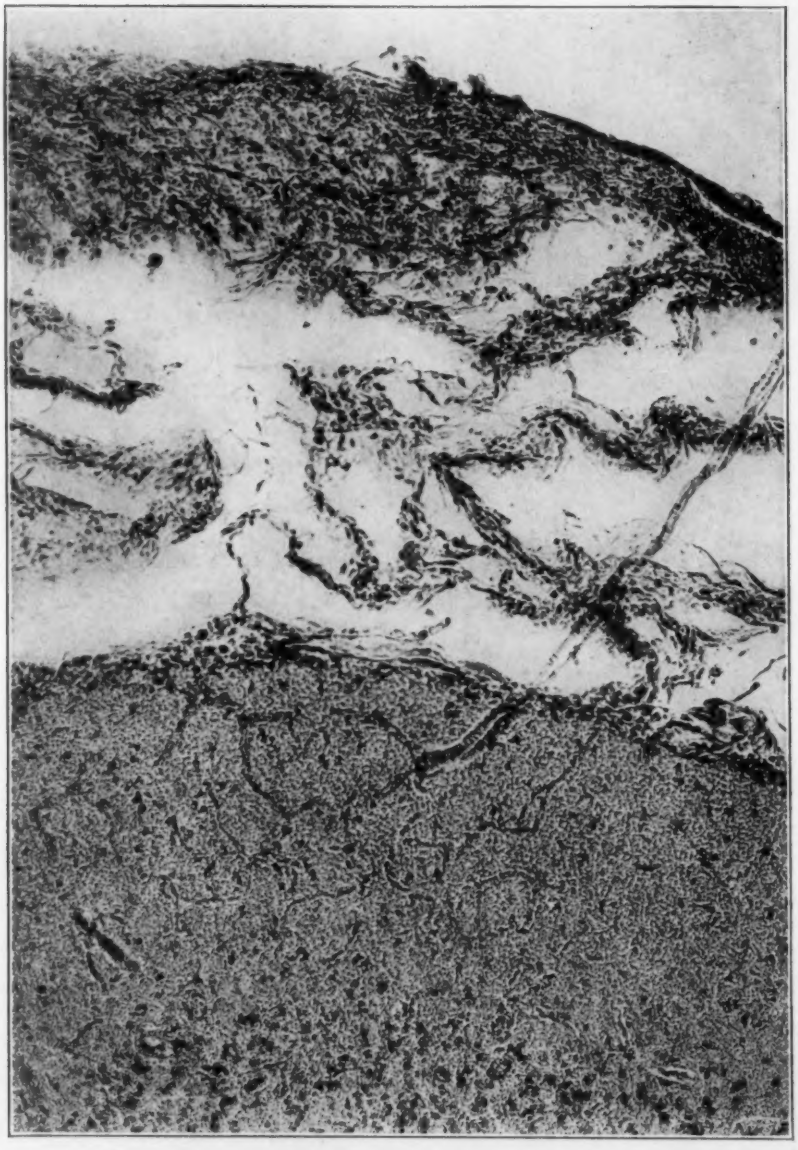

Fig. 4.—A section taken from the crest of a gyrus adjacent to the longitudinal sinus of the same dog as figure 3 showing an increase of fibrous tissue elements.

table 1) had its first convulsion forty-five days after the last injection; this seizure was followed by many others and he died during the same day. In the third pup (54, table 1), the first seizure occurred eighty days after the last injection; from this it recovered promptly and remained fairly well for seventy-two days when, without warning, there was a second series of convulsions in which the animal died. The fourth pup (56, table 1) had single convulsions ninety-three and ninety-four days after the last injection; it recovered from these. It was kept under observation eighty-seven days, during which time it did not have convulsions; but it was aggressive and ill-tempered, and was killed in a fight with another dog.

The seizures were all similar, starting with fine twitchings of a muscle group, usually the face and then spreading over the entire body.

TABLE 2.—*Protocols of the Pups with General Muscle Twitching*

Date	Amount Injected	Remarks	Lesions
Pup 59			
Feb. 28, 1927	0.8 cc. in cisterna magna	Satisfactory recovery	Moderate meningeal thickening at base
March 9	0.5 cc. in cisterna magna	Recovery	
March 28	1 cc. in cisterna magna	Recovery	
May 6	.....	Weak and sick in appearance; twitching	
May 8	.....	Weak with irregular twitching of all muscles, rhythmical twitching of the right hind leg; head drawn to right	
May 9	.....	Irregular twitching of all muscles, rhythmical twitching of right foreleg; died	
Pup 61			
Feb. 28, 1927	1.5 cc. in cisterna magna	.....	Very slight meningeal thickening at base
March 28	.....	Very poor condition; twitching, unsteady, restless and listless	
March 29	.....	Died	

The animal would soon lose consciousness and fall. The facial expression before loss of consciousness showed marked anxiety. Following the attack, the animal was dull and stupid and remained so between the seizures when they occurred in series.

In addition to the four pups which developed convulsions, two were observed forty-three and twenty-nine days, respectively, after the last injection, with severe twitchings involving all the muscles of the body without loss of consciousness. In one of these, pup 61 (table 2), the twitchings continued throughout the day; the dog was greatly weakened and died during the night. Another, pup 59 (table 2), previously well, had twitchings for three days, and on the morning of the third day was weak and twitched constantly; he died before noon. On the lateral surface of the tongue, there was a laceration which was perhaps due to biting during a general convulsive seizure in the night.

Fig. 5.—A section from the mesial wall of the hemisphere adjacent to the falx showing meningeal thickening at the top of a sulcus. The dark cells are phagocytes filled with blood pigment. At *A* two pigment filled phagocytes are seen in the perivascular space.

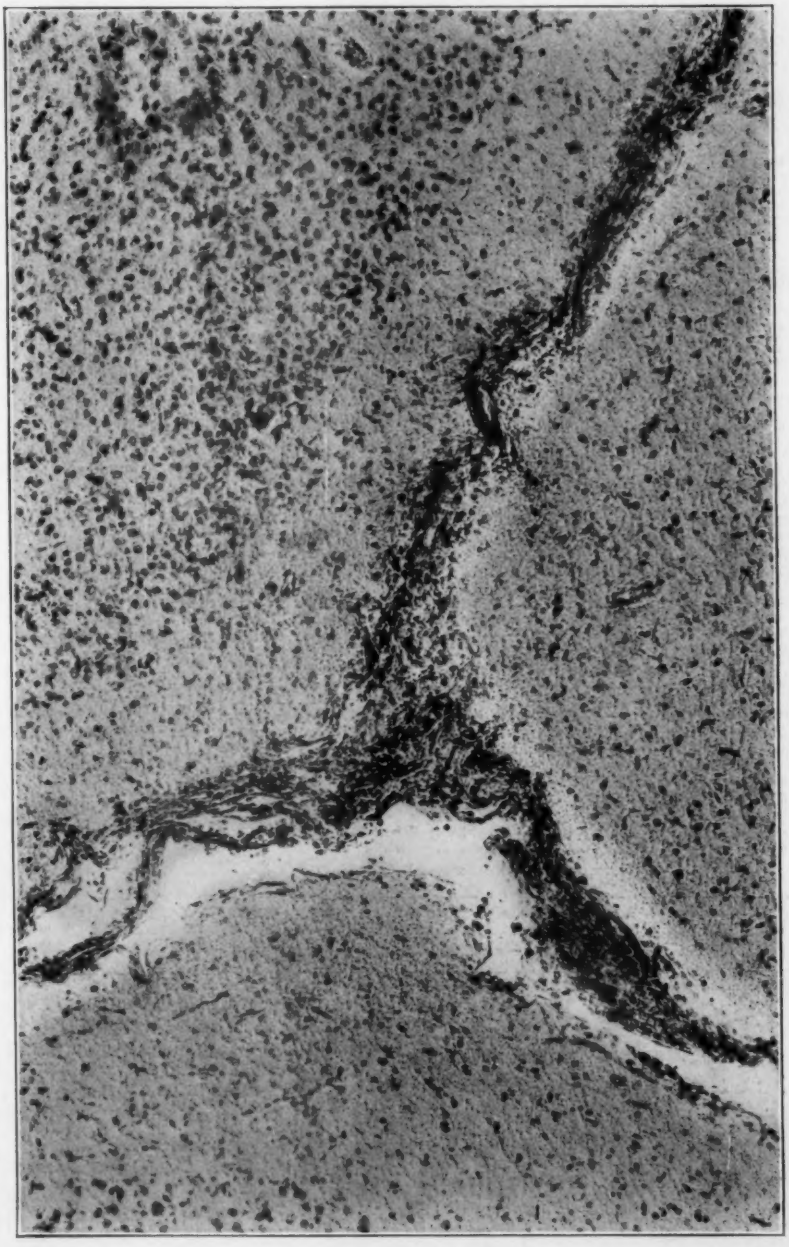

Fig. 6.—A section taken from dog 10 showing the matting together of the meninges, which is the forerunner of cortical alterations.

Convulsions or muscle twitchings were not observed in six other pups (table 3) which died from nine to sixty-three days after the injections.

In addition to the foregoing twelve puppies that died as the result of the injection, eight pups that had received injections and two controls were killed for histologic study when about half grown. Six of the pups that received injections are living and apparently well. More than one year had elapsed since the last injection was made into the six living puppies. At this time these animals do not show any ill effects resulting from the injection. They will be killed for histologic

TABLE 3.—*Protocols of the Pups Which Died Without Having Had Convulsions or Muscle Twitchings*

Date	Amount Injected	Remarks	Lesions
Pup 32			
March 26, 1926	3 cc. over right cortex	Satisfactory recovery	Meningeal thickening over cortex
April 4	.....	Died	
Pup 33			
March 12, 1926	1 cc. over right cortex	Satisfactory recovery	Moderate degree of meningeal thickening over the right and left cortex
March 26	2.5 cc. over right cortex	Satisfactory recovery	
April 4	.....	Died	
Pup 34			
March 12, 1926	1 cc. over right cortex	Satisfactory recovery	
March 23	3 cc. over right cortex	Satisfactory recovery	Meningeal thickening over cortex with some scarring
April 16	4 cc. over right cortex	Satisfactory recovery	
April 20	3 cc. over right cortex	Satisfactory recovery	
April 28	2 cc. over right cortex	Satisfactory recovery	
May 13	.....	Died	
Pup 36			
March 19, 1926	3 cc. over right cortex	Satisfactory recovery	No section; brain in poor condition when received in the laboratory
March 29	3 cc. over right cortex	Satisfactory recovery	
April 16	4 cc. over right cortex	Satisfactory recovery	
April 20	3 cc. over right cortex	Satisfactory recovery	
April 28	2.5 cc. over right cortex	Slow recovery	
May 17	.....	Died	
Pup 44			
April 23, 1926	1 cc. in cisterna magna	Satisfactory recovery	No section; brain in poor condition when received in the laboratory
June 9	.....	Died	
Pup 70			
March 28, 1927	1.25 cc. in cisterna magna	Satisfactory recovery	Moderate degree of meningeal thickening at base
May 30	.....	Died	

purposes when full grown. Of the five controls, two that were killed for histologic study seemed entirely normal at the time they were killed, and the three remaining control dogs are living and well.

LESIONS

The study of the brains of the animals that died a short time after the last injection showed grossly blood staining of the portion of the meninges with which blood had come in contact and thickening of the stained membrane. In the brains removed long after the last injection, the gross appearance varied from slight thickening of the meninges to normal. Frontal sections through the ventricles of the forebrain showed a degree of dilatation of the ventricles varying from slight to well

Fig. 7.—A section of cortex adjacent to a sulcus in which there is matting of the meninges. Active cell proliferation within the cortex is shown.

Fig. 8.—A further stage of cortical scarring following the cell proliferation as shown in figure 7.

marked. In the adult dogs, ventricular dilatation was less frequent than in the case of the pups. Of the seven adult dogs given one or more injections over the cortex and of the seven adult dogs given one or more injections into the cisterna magna, only one dog (10, table 4) showed a well marked dilatation of the ventricles (figs. 1-3). This animal was given six injections of blood into the cisterna magna over a period of thirty-nine days and was killed two days after the last injection.

TABLE 4.—*Protocols of Animals with Dilatation of the Ventricles*

Date	Amount Injected	Remarks	Lesions
Dog 10			
Jan. 23, 1925	1 cc. in cisterna magna	Satisfactory recovery	Marked meningeal thickening of meninges, at base and in some areas of cortex
Feb. 4	1.5 cc. in cisterna magna	General convulsion	
Feb. 9	1.5 cc. in cisterna magna	Slow recovery	
Feb. 18	1.5 cc. in cisterna magna	Satisfactory recovery	
March 1	2 cc. in cisterna magna	Slow recovery	
March 3	1 cc. in cisterna magna	Slow recovery	
March 5	.....	Killed	
Pup 31			
March 12, 1926	1.5 cc. over right cortex	Satisfactory recovery	Marked meningeal thickening over base and cortex
March 29	2.5 cc. over right cortex	Satisfactory recovery	
April 12	2 cc. in cisterna magna	Satisfactory recovery	
April 20	.....	Killed	
Pup 35			
March 17, 1926	3 cc. over right cortex	Satisfactory recovery	Moderate meningeal thickening at base, not much over cortex
March 24	0.5 cc. over right cortex	Slow recovery	
March 29	2.5 cc. over right cortex	Satisfactory recovery	
April 16	1 cc. in cisterna magna	Satisfactory recovery	
April 28	2.5 cc. in cisterna magna	Satisfactory recovery	
May 10	.....	Killed	
Pup 37			
March 17, 1926	3 cc. over right cortex	Satisfactory recovery	Marked meningeal thickening at base and moderate over cortex, especially at sulci
March 26	3 cc. over right cortex	Satisfactory recovery	
April 12	1 cc. in cisterna magna	Satisfactory recovery	
April 28	1.5 cc. in cisterna magna	Satisfactory recovery	
May 5	.....	Killed	
Pup 45			
April 23, 1926	2 cc. in cisterna magna	Satisfactory recovery	Very slight meningeal reaction over base
May 14	.....	Killed	
Pup 47			
April 23, 1926	1 cc. in cisterna magna	Satisfactory recovery	Moderate degree of meningeal thickening at base
April 30	2 cc. in cisterna magna	Satisfactory recovery	
May 10	.....	Killed	
Pup 70			
March 28, 1927	1.25 cc. in cisterna magna	Satisfactory recovery	Moderate degree of meningeal thickening at base
March 29	.....	Died	

Six of the nineteen puppies which had received injections and on which autopsies have been performed had definite dilatation of the ventricles (fig. 1). As shown by the protocols, all of the puppies with dilated ventricles had been given one or more injections into the cisterna magna; in addition, in some injections were given over the cortex. Two of the pups (45 and 70, table 4) received only one injection, one 2 cc. and the other 1.25 cc. of blood into the cisterna magna. One of the pups was killed twenty-one days after the last injection. The dilatation of the ventricles was always associated with meningeal thickening. Clinically, the animals did not show any evidence of the dilatation.

Fig. 9.—Active cell proliferation in the meninges covering the optic nerve. The section was taken from dog 10.

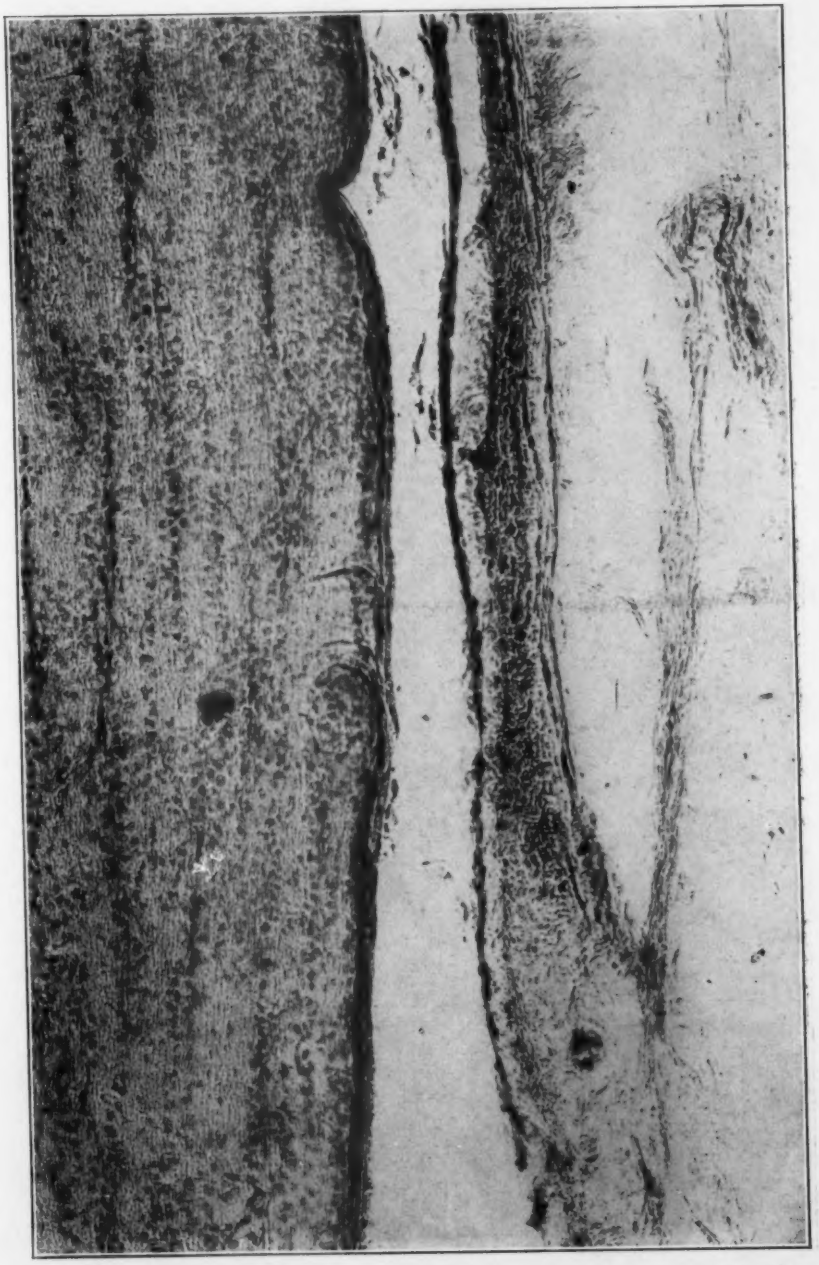

Fig. 10.—A section taken from the optic nerve of one of the control pups showing the normal meningeal coverings of the nerve.

Fig. 11.—A section from the base of the brain of pup 46 which died following convulsive seizures forty-seven days after an injection of 1 cc. of blood in the cisterna magna. There is marked meningeal thickening with cell infiltration.

The microscopic study of the brains showed meningeal thickening where blood came in contact with the membranes. In the acute stage, that is in the dogs killed soon after the last injection, the meninges showed marked cell proliferation. In figure 2, the thickened membrane is shown at the base of the brain of a dog that had been given four injections into the cisterna magna over a period of seventeen days and was killed two days after the last injection. The chronic stage of this condition is shown in figure 3, a photomicrograph from the base of the brain of an animal killed thirty-three days after the last injection. During the thirty-three days, the clinical condition was not satisfactory in that the animal ate poorly and was very weak.

This condition is not limited to the base of the brain as shown in figure 4, which is an illustration of a section taken from the same dog over the crest of the gyrus adjacent to the longitudinal sinus. The meningeal thickening is often marked at the site of sulci diminishing as the crest of the sulcus is reached. In figure 5, taken from dog 10 (table 4), the meningeal thickening at a sulcus is seen. The heavily stained cells are phagocytes filled with blood pigment. The pigment-laden cells are found even in the chronic state of the meningeal thickening secondary to the injection of blood and are useful in the microscopic examination of the specimens, as is blood-staining in the gross appearance in determining the areas of the meninges with which the blood had come in contact.

In figure 5, at *A* two pigment filled phagocytes are seen in a perivascular space well below the surface of the cortex, indicating an early stage of cortical alteration. This cortical alteration is frequently secondary to a condition seen in figure 6, where it is shown that the meningeal reaction has progressed to a point of matting together of the membranes in a sulcus, entirely obliterating the normal meningeal spaces. With a beginning cortical alteration, as seen in figure 5, active cell proliferation (fig. 7) ensues, which progresses for a time and results in fibrous tissue deposit constituting a scar, as shown in figure 8.

The meningeal reaction extends to the membranes covering the optic nerve, as shown in figure 9, a photograph of a section of the optic nerve and its coverings taken from dog 10 as compared with the same structures in figure 10, taken from one of the control puppies.

In the pups that presented symptoms and in those that died, meningeal thickening as shown in the previous sections was observed. For example, in figure 11, taken from the base of the brain of pup 46 (table 1), the meninges are thickened and contain a large amount of fibrous tissue. A photograph (fig. 13) taken from the occipital pole of the brain of pup 54 shows the meninges of a sulcus in active cell proliferation extending into the cortex at the site of a blood vessel.

Fig. 12.—A section of the meninges from the base of pup 59 which died during convulsions forty-two days after receiving three injections of blood into the cisterna magna showing an increase of fibrous tissue elements.

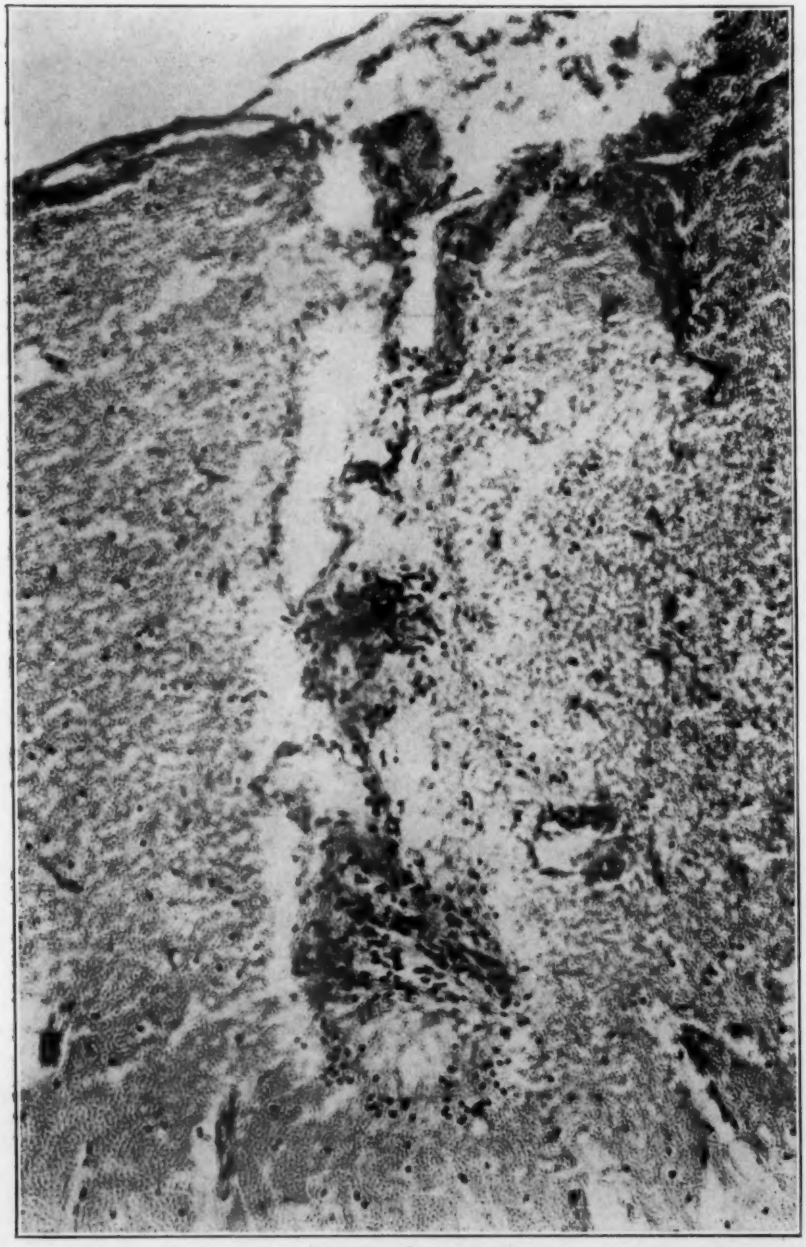

Fig. 13.—A section taken from the occipital pole of pup 54 showing meningeal thickening in a sulcus with beginning cortical alteration.

CONCLUSIONS

Blood mixed with the cerebrospinal fluid of young and adult dogs produces neurologic disturbance varying from slight difference in behavior to severe convulsive seizures. Though some of the animals were severely affected by small quantities of blood mixed with the cerebrospinal fluid, others have survived more than a year, and are apparently normal.

Following the introduction of blood into the cerebrospinal fluid, there begins a reaction of the parts of the meninges which have come in contact with the blood. The meningeal reaction tends to subside and may disappear as the blood disappears from the fluid. After several weeks, the cell elements are less numerous in the meninges, but a large amount of fibrous tissue is present.

Late in the course of the meningeal reaction, changes in the structure of the cortex are observed.

Moderate dilatation of the ventricle not infrequently occurs following the introduction of blood into the cerebrospinal fluid of young pups. The condition may occur in adult dogs, but with less frequency.

These facts as applied to patients with bloody cerebrospinal fluid are discussed in part B of this paper.

This work has been carried on under the direction of Dr. Adolf Meyer. Dr. Frank Ford assisted in some of the experiments and Miss Cecelia Bisson in the making of the motion picture films, for the study of the behavior of the animals, and in making the illustrations for this paper.

BLOOD IN THE CEREBROSPINAL FLUID

RESULTANT FUNCTIONAL AND ORGANIC ALTERATIONS IN THE CENTRAL NERVOUS SYSTEM *

B. CLINICAL DATA

CHARLES BAGLEY, JR., M.D.
BALTIMORE

In a report concerning some experiments made to determine the effect of a relatively small amount of blood in the cerebrospinal fluid,[1] attention was directed to the acute and chronic symptoms resulting from the meningeal irritation caused by the blood. The present report concerns some experiences with bloody cerebrospinal fluid in patients ranging in age from a few days to 56 years who presented meningeal lesions similar to those produced in the experiments.

The sudden appearance of blood in the cerebrospinal fluid of the very young or of middle-aged persons is rare enough to excite one's curiosity as to the cause of the bleeding. The first part of this paper deals with the examination of the brains in some of the fatal cases and the lesions responsible for the blood.

REPORT OF CASES

CASE 1.—*Venous plexus of cerebellar pia; drainage of cerebrospinal fluid without benefit.*

Baby G. was admitted to the hospital when 16 days old. Labor was uncomplicated, and the child seemed normal in every way until 15 days old, when the mother noticed twitchings of the muscles of the body, drawing back of the head and rolling of the eyes. The following day there were several severe convulsions. Lumbar puncture, performed when the patient was admitted to the hospital, showed bloody cerebrospinal fluid. The drainage of this fluid did not improve the condition, and on the following day an opening was made in the right temporal region. When the dura was incised, there was little cerebrospinal fluid in the subarachnoid space, the cortical veins were dilated, and old blood was seen. The absence of cerebrospinal fluid was in striking contrast to the condition usually found in simple hemorrhages at birth. Drains were inserted beneath the dura. Following the operation there was not the usual free drainage of cerebrospinal fluid, and several lumbar punctures were made. In all of these punctures the fluid was bloody, and eighteen days after the operation it was concluded that a large blood clot was present. As there was no indication of the location of the supposed clot, further exploration was not attempted, treatment was

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* From the Neurological Laboratory of the Henry Phipps Psychiatric Clinic, Johns Hopkins University.

* Read before the Southern Surgical Association, Augusta, Ga., December, 1927.

1. Bagley, C., Jr.: Blood in the Cerebrospinal Fluid: Resultant Functional and Organic Alterations in the Central Nervous System. A. Experimental Data, Arch. Surg., this issue, p. 18.

abandoned, and the child died fifty-one days after birth. Autopsy revealed a venous plexus covering the greater portion of the cerebellar cortex (fig. 1) and marked dilatation of the ventricle as shown in figure 2.

On section, the pia was seen to be much thickened and contained a great many dilated, thin-walled veins, as shown in figure 3. The sudden appearance of symptoms was due to rupture of a vein. Repeated punctures failed to clear the fluid because of recurrent bleeding from this source. The dilatation of the ventricles was due to the adhesions at the foramina of Magendie and Luschka. Hydrocephalus secondary to hemorrhage in the posterior fossa has been described by Arthur G. Jacobs[2] in the case of a new-born child with early evidence of hemorrhage. Seventy-five days after birth, suboccipital exploration by Dr. R. E. Semmes revealed extensive adhesions and arrested the condition.

Fig. 1 (case 1).—Greater part of the cerebellum is covered by a network of veins. Rupture of one of these veins was the cause of the hemorrhage fifteen days after birth.

CASE 2.—*Venous plexus involving chiefly the occipital and cerebellar veins; extravasation of a small amount of blood from a cerebellar vein with signs of increased intracranial tension.*

M. H., a girl, aged 20, had a history of normal development until the age of 6 years, when she had had a severe attack of measles, since which time she had not been strong. At the age of 12, she was extremely ill with influenza, and at that time a heart murmur with cardiac enlargement was found. At the age of 16, a murmur was first heard in the head. During the four years preceding the examination, headache was troublesome; it became severe after an attack

2. Jacobs, A. G.: Hydrocephalus Following Intracranial Hemorrhage, South. M. J. **19**:669 (Sept.) 1926.

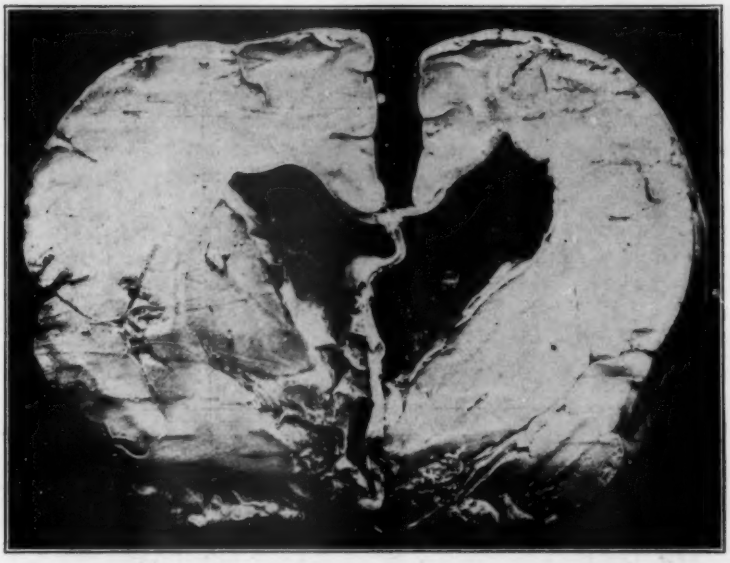

Fig. 2 (case 1).—The frontal section of the brain showing marked dilatation of the ventricles secondary to hemorrhage in the posterior fossa.

Fig. 3 (case 1).—Showing one of the many dilated thin-walled veins covering the cerebellar cortex.

of otitis media twelve weeks before the examination, at which time a mild degree of choked disk was noted. These facts suggested the possibility of an abscess of the brain. Two weeks before the examination, while stooping to fasten her galoshes, she was suddenly aware of a brushing sound, which she thought was caused by some one passing her in the room. This was immediately followed by a severe headache, vomiting and dizziness. Lumbar puncture ten days later showed marked increase in pressure and evidence of a small amount of old blood in the cerebrospinal fluid. When examined four days after this puncture, the patient was stuporous but could be aroused. The examination revealed a loud systolic murmur over the precordium extending into the neck and a loud bruit over the entire head synchronous with the heart beat. There

Fig. 4 (case 2).—The posterior part of the skull including the occipital and part of the parietal bones, showing the deep depressions corresponding to the greatly dilated venous sinuses and tributaries.

was marked spontaneous nystagmus and a high degree of choked disk. The diagnosis of a cerebral vascular lesion, exact type unknown, with leakage of blood into the cerebrospinal fluid was made. Because of the likelihood of exciting further bleeding, a lumbar puncture or a more radical operative procedure was not undertaken. Two weeks later, the patient was in a serious condition because of increased intracranial pressure, and she died twenty-four hours after an attempt at relief through a right subtemporal decompression.

Postmortem examination showed that the lesion involved chiefly the venous structure of the dura, resulting in deep channeling of the skull as shown in figure 4. In the left cerebellar pontile angle, several dilated and recently

thrombosed veins were seen (fig. 5). Sections of the area of extravasation showed several thin-walled veins (fig. 6). A large clot was not found; the marked increase in intracranial pressure was evidently due to the irritation of the bloody cerebrospinal fluid. Leakage had, no doubt, been occurring over a period of fifteen weeks, corresponding to the course of the final illness.

CASE 3.—*Recurrent hemorrhage following rupture of an aneurysm of the anterior cerebral artery, with signs of increased intracranial tension.*

E. S., a girl, aged 12, entered the hospital with a history of a sudden severe headache thirty-five days before admission. The headache was associated with vomiting. A week later, because of continuance of symptoms, she was admitted to the Western Maryland Hospital in Cumberland, and lumbar puncture at that time revealed bloody cerebrospinal fluid. Twelve days later, she was discharged from the hospital with marked improvement in symptoms, though she was rather dull and vision was blurred. Thirty-one days after the first attack of headache, she had a second severe attack with two general convulsive seizures, diplopia and

Fig. 5 (case 2).—Marked venous dilatation with recent thrombus in the cerebellar pontile angle.

badly blurred vision. Five days later, she was admitted to the Church Home and Infirmary, Baltimore, where I first saw her. At the time of admission, there was severe headache, vomiting and stupor (though she could be aroused) and a very high grade choked disk, with hemorrhages; the right pupil was larger than the left, and a loud cerebral bruit was heard over the entire head, but more distinctly in the temporal regions. When questioned, the child said that she had heard the murmur for a long time. Bloody cerebrospinal fluid was obtained on lumbar puncture. A right subtemporal decompression for relief of pressure was made, and the child died four days after operation. Figure 7 shows a large hemorrhage between the hemisphere extending into the left lateral ventricle. Microscopic study of this area showed an organized blood clot, the result, no doubt, of the bleeding which caused the original attack thirty-five days before admission to the hospital, a large amount of recent hemorrhage and an aneurysmal dilatation of the right anterior cerebral artery (fig. 8). Rupture of the aneurysm was the cause of the bleeding.

Fig. 6 (case 2).—A higher magnification of the vein in figure 5, showing the breaking down of the thin wall of the vein and recent thrombus.

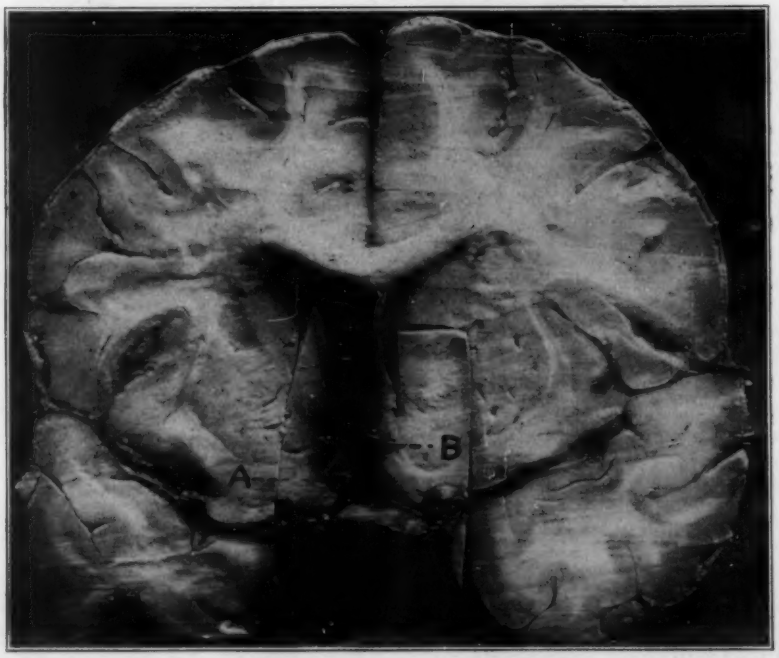

Fig. 7 (case 3).—Between the hemispheres there is a blood clot extending from the base into the left ventricle. At *A*, the cut end of the left anterior cerebral artery is seen; at *B*, an aneurysm of the right anterior cerebral artery.

CASE 4.—*Hemorrhage due to rupture of an aneurysm of the anterior cerebral artery. Death followed the initial rupture.*

C. B., a man, aged 37, previously in good health, was suddenly seized with severe headache and vomiting, followed almost immediately by coma. He died

Fig. 8 (case 3).—Section from figure 7. *A*, indicates the left anterior cerebral artery. The right anterior cerebral artery is ruptured; the elastic tissue extends between *B* and *C* to the right. Upward from *B* and *C*, the aneurysm extends as far as *D*.

eight hours after the onset. There was no history of a cerebral bruit or other indication of the aneurysm before the final attack. Autopsy showed a large amount of free blood within the cranium and a clot in the left frontal lobe. The frontal

section of the brain, as seen in figure 9, showed a bulbous enlargement of the anterior cerebral artery. Sections of this unruptured aneurysm are shown in figures 10 and 11. This lesion was not the source of the hemorrhage; a second small aneurysm of the artery ruptured subcortically. Small aneurysms of this type are frequently multiple.

CASE 5.—*Recurrent hemorrhage following rupture of an aneurysm of the anterior cerebral artery.*

M. H., a man, aged 41, was admitted to the hospital complaining of headache and weakness of the left side of the body. The illness began three months before admission with sudden loss of consciousness. Five weeks after the onset the patient again lost consciousness, and there was paralysis of the left side of the body; this gradually improved until the time of admission to the hospital. The

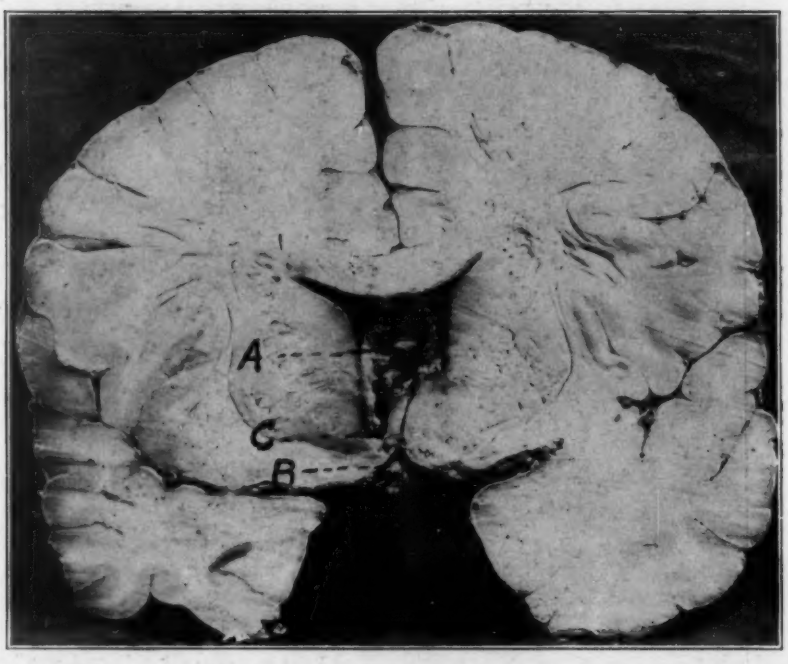

Fig. 9 (case 4).—*A* shows blood clot resulting from the rupture of a branch of the left anterior cerebral artery at *C*. *B* indicates aneurysm of the anterior cerebral artery unruptured, shown in figure 10.

examination showed partial hemiplegia of the left side and arteriosclerosis. The Wassermann test of the blood and spinal fluid was negative, and the spinal fluid contained 13 cells. Four days after admission to the hospital, the patient suddenly lost consciousness, but he improved during the following hour, at which time there was complete loss of power of all muscles of the left side of the body. He again lost consciousness and died two hours after the onset of the attack. The history did not mention a cerebral bruit, so that it is not possible to say whether or not one was present. Autopsy showed general arteriosclerosis, free blood over the right cerebral cortex and a partially organized blood clot at the base between the hemispheres of the brain anterior to the chiasm, as shown in figure 12.

Section of the blood clot showed an aneurysm of the right cerebral artery as shown in figure 13.

CASE 6.—*Recurrent hemorrhage in a patient at the age of 22, 42 and 44 years; large calcified mass at the site of the first hemorrhage and beginning calcification in the second with an aneurysm of the anterior cerebral artery; death two hours after the third hemorrhage.*

Fig. 10 (case 4).—A section of the aneurysm shown at *B* in figure 9, with the elastic fiber stained by Verhoeff method. The extent of the vessel wall is indicated by the dark line of elastic tissue between *A* and *B* below which the aneurysm extends.

E. A., a man, aged 42, first came under observation in June, 1926, complaining of headache, drowsiness, slight loss of memory and some weakness of the extremities. In walking, he leaned forward and was careless in raising his feet. The symptoms had gradually been increasing over a period of three weeks. There

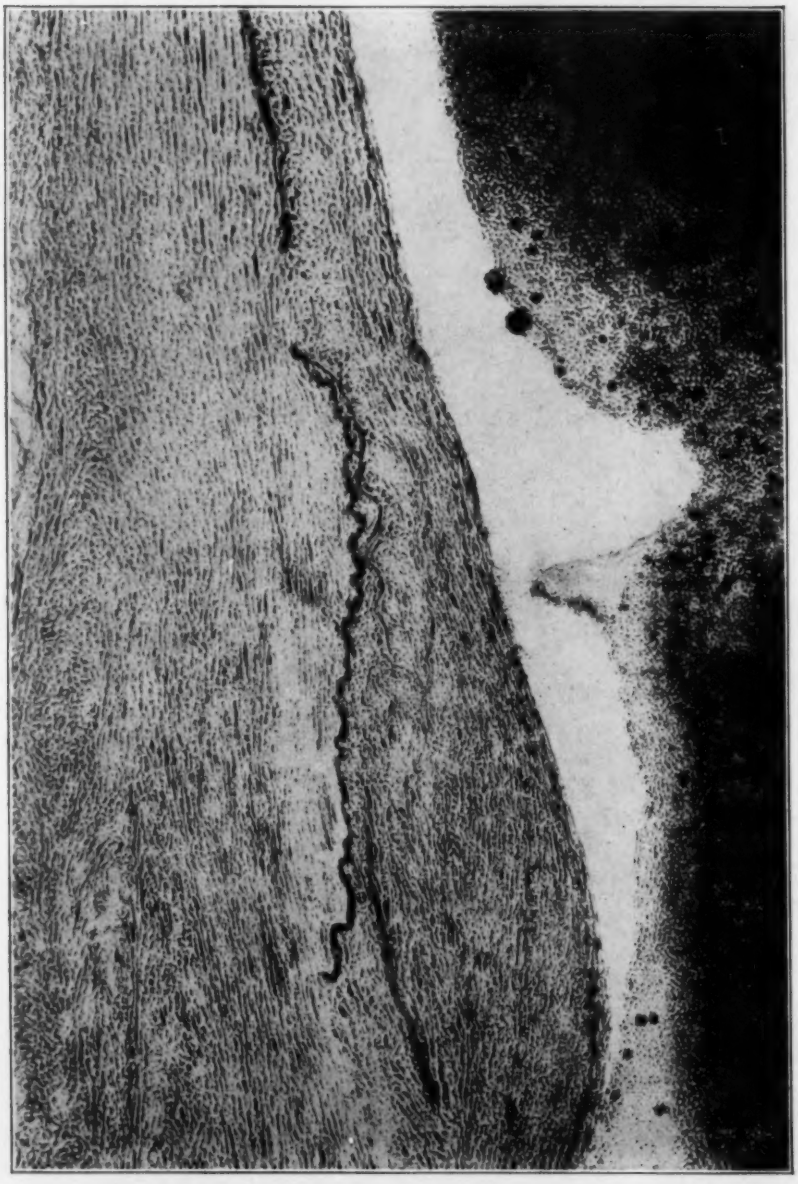

Fig 11 (case 4).—Higher magnification (× 125) of *A* in figure 10, showing the abrupt termination of the elastic tissue.

was a mild degree of choking of both optic nerves. The roentgenogram showed a smooth, calcified mass 1 cm. above and not connected with the sella turcica (fig. 14). In the anteroposterior view, this mass was seen exactly in the midline (fig. 15). The patient said that at the age of 22 he had had a similar illness which had necessitated his remaining in bed for six weeks, but he had entirely recovered. This fact led to the opinion that the calcified mass shown in the roentgenogram had to do with the previous illness. The smooth external surface of the mass suggested calcification in a cyst, and tumor calcification was ruled out. Soon after the patient's admission, the symptoms improved, and he was discharged from the hospital on the twenty-second day. In spite of the fact that a bruit was not heard and a lumbar puncture could not be made because of the danger of exciting further bleeding, it was concluded that the patient had a vascular lesion and that the attacks were due to bleeding as had been found in

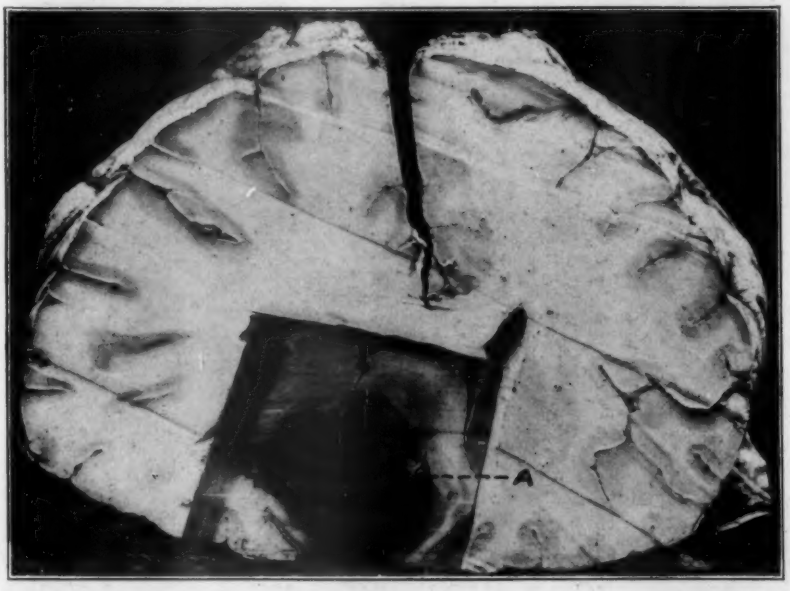

Fig. 12 (case 5).—Blood clot between the frontal lobes with the left anterior cerebral artery at *A*.

the foregoing case. After leaving the hospital, the patient remained off duty, avoiding physical strain as far as possible and returned to his office work six months later. From this time he was free from symptoms until Jan. 13, 1928, when a large hemorrhage occurred which caused death two hours later.

Autopsy showed the cerebral ventricles dilated and filled with fresh blood. The calcified mass bulged into the ventricles covered by a thick membrane as shown in figure 16. In figure 17, a cross-section of an aneurysm is shown at *A*. The left wall of the aneurysm was thick, while the right portion was thin and marked the point of leakage. The thin right wall was separated from the brain tissue by a recent blood clot which was the most anterior portion of the large clot which filled the ventricles. Below the cavity at *B*, there was an organized cyst which extended from this point caudalward, a distance of 1.5 cm. This, no doubt, was the site of the hemorrhage which occurred almost two years before

Fig. 13 (case 5).—Section taken from the area of blood clot in figure 12, showing the left anterior cerebral artery at *A* and the right anterior cerebral artery with an aneurysmal dilatation. The termination of the elastic tissue marking the extent of the arterial wall is shown at *B* and *C* below which the aneurysm extends.

Fig. 14 (case 6).—Above the sella turcica a calcified mass is seen.

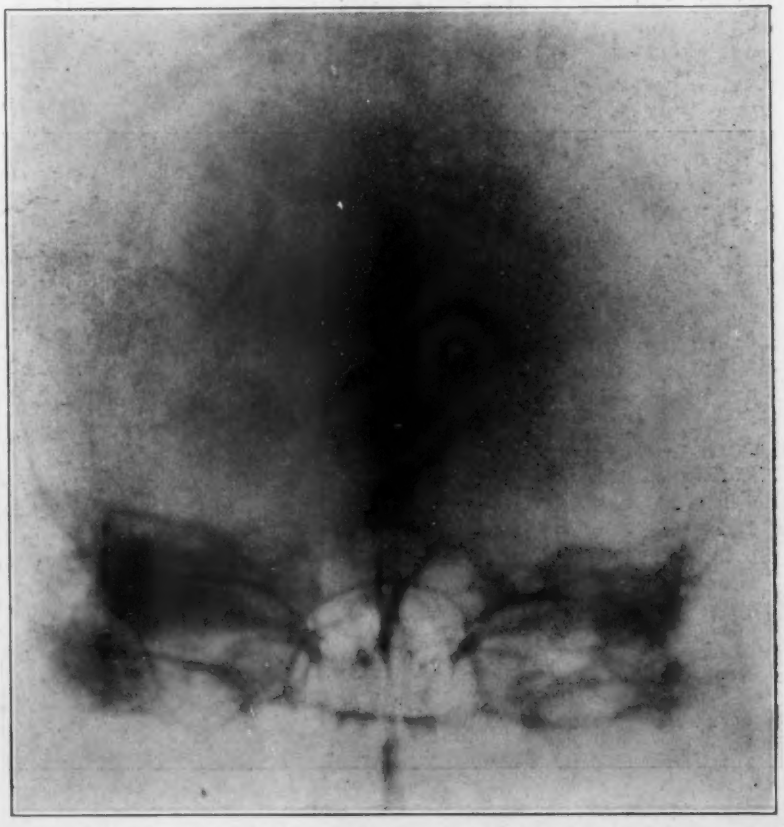

Fig. 15 (case 6).—Anterioposterior view showing midline position of calcified mass.

Fig. 16 (case 6).—Frontal section showing dilatated ventricles which were filled with fresh blood and the calcified mass at *A* shown in figures 14 and 15.

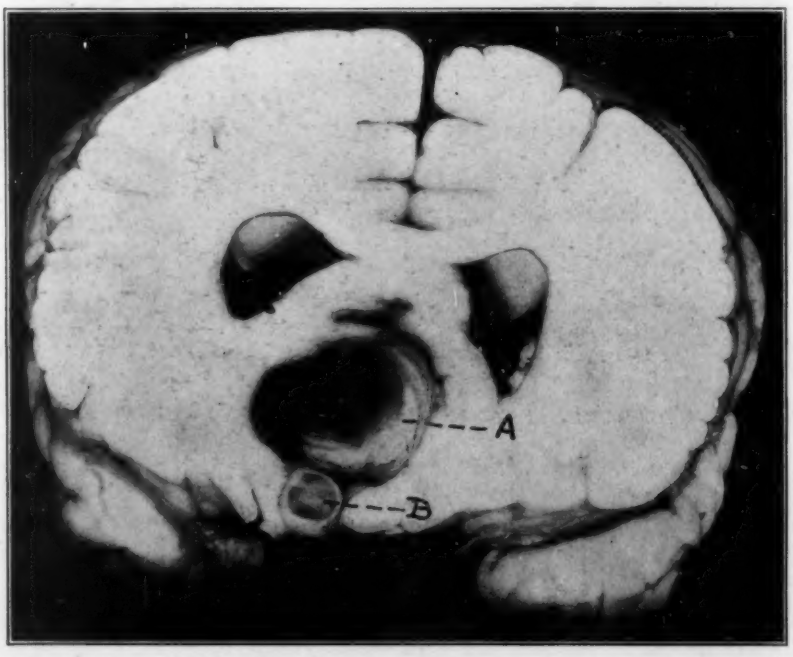

Fig. 17 (case 6).—Anterior cerebral aneurysm at *A* and calcified cyst at *B*.

death. In the wall of this mass beginning calcification was seen, and it is probable that this would have been similar to the large calcified mass if the patient had survived. In figure 18, the anterior cerebral artery at the caudal extremity of the aneurysm is shown. The thick wall of the aneurysm in this

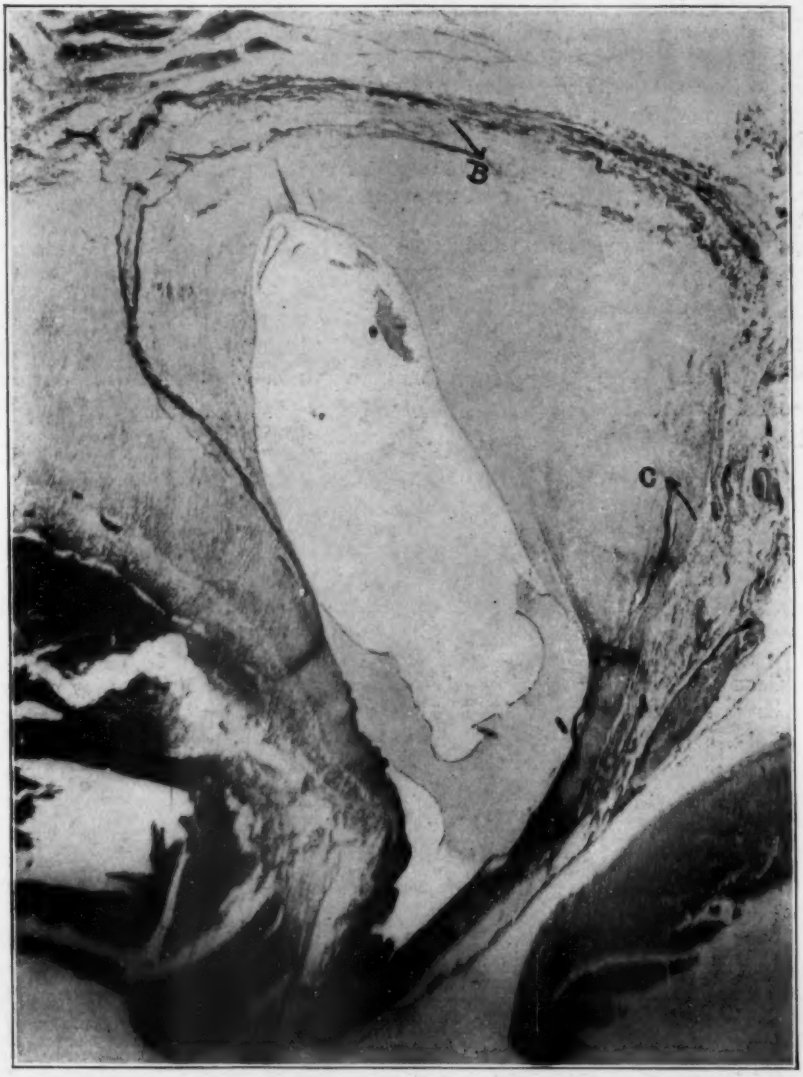

Fig. 18 (case 6).—Anterior cerebral artery at its junction with the aneurysm shown at *A* in figure 17. The elastic tissue present from *B* to *C* is absent between the points of the arrows.

section was lacking in elastic tissue. Sections through the large sac as shown in figure 17 also demonstrated complete absence of elastic tissue.

CASE 7.—*Clinical evidence of hemorrhage in the same area as shown in the three preceding cases in which the patients recovered following the initial attacks.*

Mrs. R. R., a woman, aged 34 years, while walking with her husband in the garden, suddenly exclaimed, "I have the funniest feeling in my head and it hurts. I am going into the house and lie down." I saw this patient three days later, when stupor, nausea and vomiting, marked bilateral edema of the disks with hemorrhages and abducens weakness were present. The cerebrospinal fluid, as obtained by lumbar puncture, was slightly bloody. Only a small amount of fluid was taken, and the puncture was not repeated because of the presence of choked disk and the possibility of exciting further bleeding. A cerebral bruit was not heard. The symptoms progressed for two days, when there was paralysis involving chiefly the muscles of the right side of the body. The paralysis and choking slowly disappeared, but there was some headache for two months. It is now eight months since the onset of the illness, and the patient is free from symptoms; however, there is grave danger of recurrence of the symptoms.

Until recent years, cerebral aneurysms have been mainly of pathologic interest. Five years ago, Dr. C. P. Symonds and Dr. Harvey Cushing [3] called attention to the importance of clinical facts concerning these lesions. Slight hemorrhage with definite clinical manifestations usually precedes the large fatal hemorrhage in small cerebral aneurysms and must be considered in the differential diagnosis of obscure lesions of the brain.

The source of bleeding in infants is a matter of great importance. The bleeding is frequently due to tearing of the large dural sinuses, but in some cases it is probably due to tearing of the cortical veins as they enter the dura. The following case is included because of its course which typifies what happens when blood escapes into the cerebrospinal fluid and because of the specimen which shows the source of the blood.

CASE 8.—*Small amount of blood in the cerebrospinal fluid following cerebral trauma; death in status epilepticus on the third day.*

J. D., aged 6 months, was in excellent physical condition when left with a colored nurse. When the mother returned two hours later, the child was unconscious and the nurse did not give any indication of the cause. Twenty-four hours later the fontanel was tight, and there was a severe general convulsive seizure. Seizures occurred at short intervals until collapse eighty hours after the onset when the child died. Lumbar puncture during the third day revealed bloody cerebrospinal fluid.

Autopsy showed a moderate amount of blood mixed with the cerebrospinal fluid and a small blood clot over the left frontal cortex where a vein had been torn from the dura (fig. 19). The pia-arachnoid was thickened and the veins markedly dilated.

CASE 9.—*Tumor of choroid plexus with hemorrhage into ventricle on the tenth day. The early date of bleeding created confusion with birth hemorrhage.*

H. M., came under observation when 10 days old because of sudden increase in intracranial pressure, with vomiting, respiratory embarrassment and loss of consciousness. When the patient was examined about six hours after the onset

3. Symonds, C. P.: Clinical Study of Intracranial Aneurysms, Part 1, Guy's Hosp. Rep. **73**:139 (April) 1923. Cushing, H.: Clinical Study of Intracranial Aneurysms, Part II, ibid. **73**:159 (April) 1923.

of the symptoms, the fontanel was bulging and tense, and the cerebrospinal fluid contained a large amount of blood. The late onset of the symptoms without any indication of a hemorrhage during the first hours after birth and the quantity of fresh blood in the cerebrospinal fluid led to the suspicion of a lesion similar to that shown in case 1. Repeated lumbar punctures showed a gradual decrease in the amount of the blood, but the fluid remained yellow, and normal intracranial

Fig. 19 (case 8).—Specimen from an infant, aged 6 months, showing blood clot at the site of a torn cortical vein at point of attachment to dura. The clot is small and merely marks the point of escape of blood into the cerebrospinal fluid, which produced severe convulsive seizures and death.

Fig. 20 (case 9).—Tumor of the brain, the source of a large amount of blood in the cerebrospinal fluid on the tenth day after birth.

tension could not be maintained. At the age of 9 weeks the circumference of the head was 40 cm., the fontanel was large and the sutures were separated. With the view to determining the possible presence of hydrocephalus, air was introduced through a lumbar puncture needle. Only the right ventricle was filled.

The right ventricle was then aspirated and air was injected, but again only the right ventricle was filled. A left osteoplastic bone flap was removed and a large solid tumor uncovered. The flap was replaced, and the child died twelve days later.

Examination of this tumor, shown in figure 20, proved to be a choroid plexus growth. The foramen of Monro was entirely occluded, and part of the left

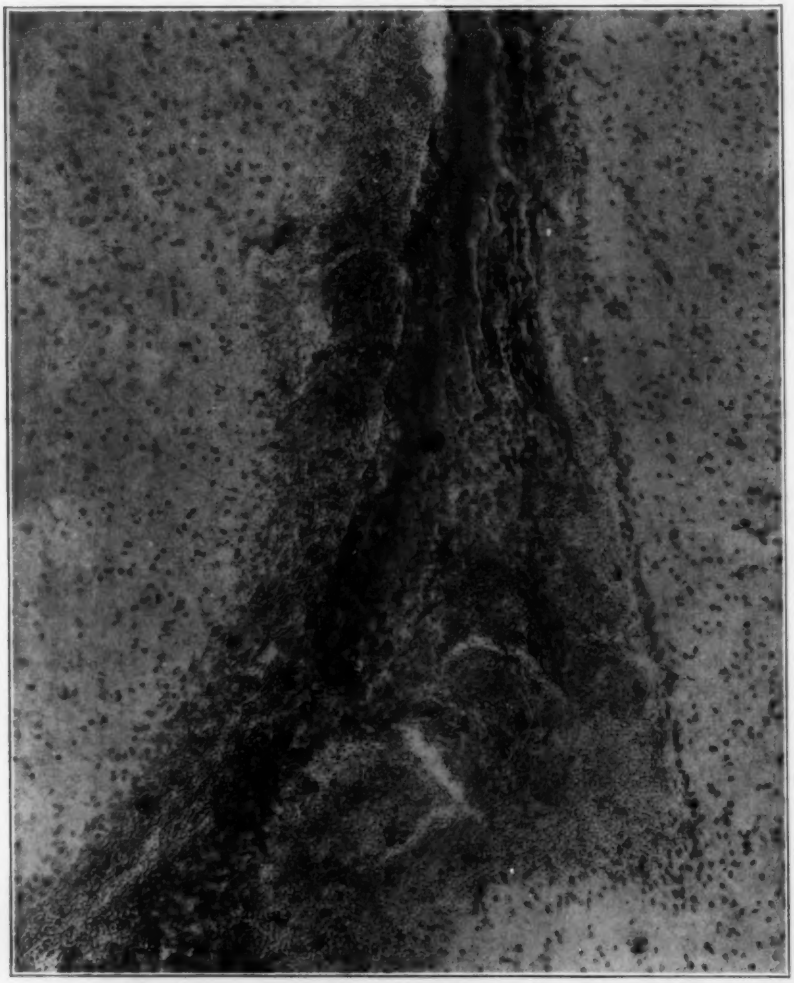

Fig. 21 (case 10).—Cerebral meningeal reaction resulting from bloody cerebrospinal fluid due to injury of the spinal cord.

lateral ventricle of the forebrain which was not filled with tumor was greatly distended with blood-stained fluid.

CASE 10.—*Cerebral irritation following bloody cerebrospinal fluid, extracranial source of blood with no likelihood of cranial injury.*

The case of Baby B. is interesting because the injury at birth which was the source of blood was in the spinal cord, the blood reaching the cerebral sub-

arachnoid space in the same manner as in the experiments on dogs when the injections were made into the cisterna magna. The child was born after breech delivery and weighed 9 pounds (4.1 Kg.). From the beginning the condition was not satisfactory, and twelve hours later the temperature was 107 F. The fontanel was bulging slightly, and bloody cerebrospinal fluid was obtained on lumbar puncture. When 36 hours old, the child had two general convulsive seizures and died. The injury of the cord involved the eighth cervical and the first thoracic segments; from this point, blood had reached the cerebral cortex, producing marked clinical disturbance and the first stage of meningeal reaction shown in figure 21.

CASE 11.—*Chronic meningitis in which the clinical course and observations at autopsy suggest early bloody cerebrospinal fluid.*

Fig. 22 (case 11).—Arachnoid mesh at the fissure of Sylvius which before fixation in formaldehyde was greatly distended with cerebrospinal fluid.

M. B., aged 9 months, had had a normal birth and did well until the age of 2 months, when she was irritable and cried a great deal. The feeding was thought to be the cause, but frequent changes in the diet did not improve the condition. Vomiting was troublesome, and there was gradual increasing rigidity. When 6 months old, she had a severe general convulsion, following which the condition grew worse. When admitted to the hospital at the age of 8½ months, the child was undernourished and spastic, it had convulsive movements of the arms and legs, and the head was retracted. The cerebrospinal fluid was clear, with 2 cells per cubic millimeter. When the patient was admitted to the hospital, the temperature was 101.5 F., and it ranged between this and 107 F. until death two weeks later.

Fig. 23 (case 11).—A section from the base of the brain of an infant with clinical evidence of bloody cerebrospinal fluid showing meningeal thickening.

Autopsy revealed chronic meningeal thickening; the arachnoid at the sulci was opaque and edematous; in the sylvian fissure, it had the appearance of a veil-like sponge filled with fluid. In figure 22, the arachnoid mesh in which the fluid was held is shown; fixation of the tissue had caused the membrane to shrink below the level of the surrounding cortex in marked contrast to the distended membrane when seen in the fresh state. The meningeal thickening at the base of the brain is shown in figure 23.

My interest in the subject of bloody cerebrospinal fluid began during the summer of 1923, when the following case came under observation.

CASE 12.—*Chronic meningitis, secondary to birth hemorrhage (clinical evidence). Gradual increase in the head and other indications of hydrocephalus.*

Fig. 24 (case 12).—Chronic meningeal thickening with marked dilatation of the cortical veins.

Ventricle normal in size, a large amount of fluid over the cerebral cortex. Subtemporal decompression greatly diminished the meningeal thickening on the side drained, but had no influence on the undrained side.

P. C., aged 27 months, was apparently normal at birth. Jaundice was present on the second day and lasted for some weeks. Vomiting was troublesome on the fifteenth day and had continued irregularly, making it difficult to keep up body nourishment. At the time of the examination, the child weighed 22 pounds (10 Kg.). The appearance of the head indicated hydrocephalus, the fontanel was large, circumference 48 cm., thin, fine hair was present over the scalp, and there was internal squint of both eyes. Air injected into the ventricles showed both ventricles to be of normal size, but a large amount of air escaped over the cortex. A right subtemporal decompression revealed large cortical veins which were matted together, especially in the sylvian fissure. The arachnoid was thickened and

opaque. There was a large amount of cerebrospinal fluid over the cortex. A drain was inserted, and following the operation there was free drainage of cerebrospinal fluid which continued even after removal of the drain. The child died of pneumonia twenty-two days after the operation. The particular interest in this case is found in the examination of the brain, first because of the undilated ventricles in a child with a large head and other indications of hydrocephalus; second, because of the difference in the meninges and meningeal vessels on the drained and undrained sides of the brain. Grossly, the drained side was lighter in color than the undrained side, which was dark and cyanotic, suggesting a venous stasis. The veins of the undrained side were large, and small tributaries were plainly visible (fig. 24), while on the drained side (fig. 25) the veins were smaller, and the tributaries were not seen. Microscopically, the pia-arachnoid was much

Fig. 25 (case 12).—The opposite side of the brain shown in figure 24. When explored twenty-two days before death this hemisphere had the same appearance as that shown in figure 24. Free drainage of cerebrospinal fluid during the interval between operation and death greatly improved the drained side, but seemed to have had no influence on the undrained side.

thickened, the walls of the vessels were heavy and they were dilated on the undrained side. The difference in the membrane at the top of a sulcus is shown in figures 26 and 27. Deep in the sulci, the changes were marked. In figure 28, taken from the undrained side, there is a large amount of fibrous tissue and the vessel walls are thick in sharp contrast to the more delicate arrangement of these structures in figure 29, taken from a sulcus of the drained side. The lesions shown in the examination of the meninges of this brain were like those found in the young dogs following the injection of blood in the cerebrospinal fluid, and were similar to those found in verified cases of bloody cerebrospinal fluid in infants which in some instances presented the same clinical picture so that it

seems fair to assume that this child had a hemorrhage, though lumbar puncture was not performed early.

In its most simple form, bloody cerebrospinal fluid is seen in a type of hemorrhage in the new-born. Such cases show a disturbance ranging from twitching to general convulsive seizures during the first few days immediately following delivery. The story of hemorrhage in the

Fig. 26 (case 12).—The dilated vessels and thickened arachnoid mesh on the undrained side.

new-born has been told many times and need not be repeated here, so that only a few cases illustrating types of cases and methods of treatment are included.

CASE 13.—*Small amount of blood in the cerebrospinal fluid during birth, with mild cerebral disturbance; entirely controlled by repeated lumbar punctures.*

Baby J. F. B., a breech delivery, was apparently normal until about 24 hours of age, when he became limp and cyanosed and had attacks of twitching involving the whole body. These twitchings occurred at intervals of from two to three hours. A lumbar puncture was made on the third day, and yellow cerebrospinal fluid was obtained. The following day there was no improvement in the condition, and a second lumbar puncture was performed. The fluid obtained was more

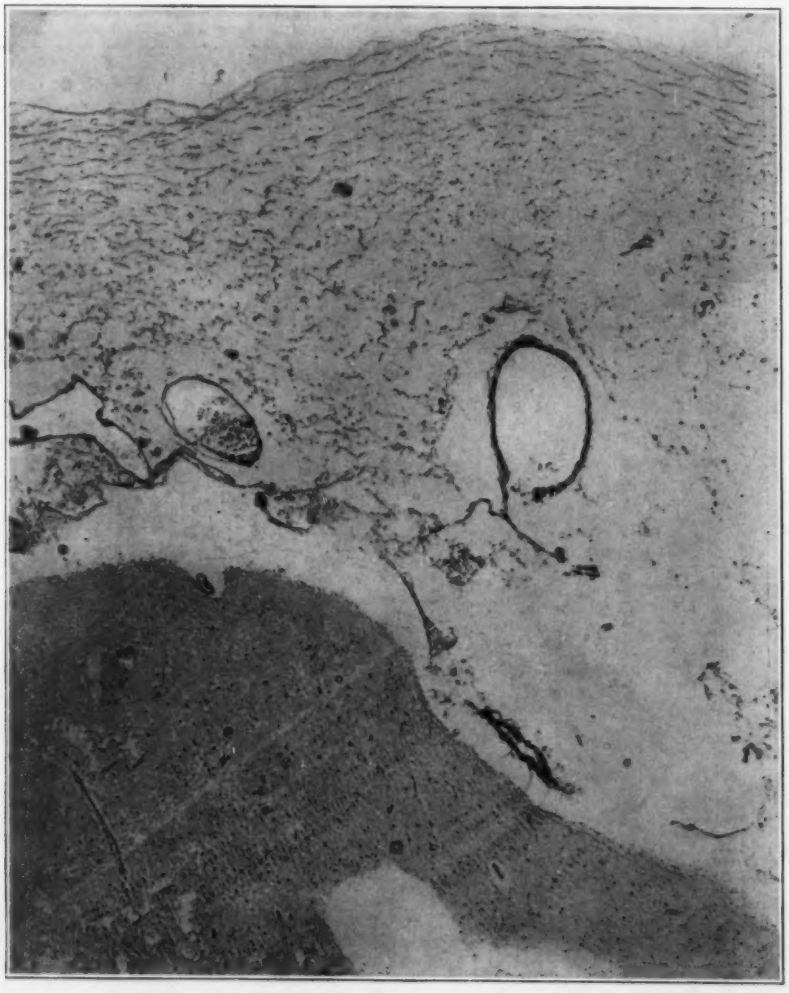

Fig. 27 (case 12).—Pia-arachnoid on the crest of a gyrus near a sulcus, showing the more delicate arachnoid mesh than in figure 26.

deeply tinged than that withdrawn at the first puncture. During the observation, there were constant jerkings of the entire body—more marked in the left arm. After the second puncture, there was marked improvement in the condition, with milder attacks occurring at longer intervals. On the fifth day, lumbar puncture revealed a more deeply stained cerebrospinal fluid. The fluid flowed without any evidence of pressure. Attacks were not noted after the fifth day. Several

punctures were made during the latter period of the stay in the hospital, and the fluid gradually returned to a normal color.

This child is now entirely normal at the age of 27 months.

With a history such as that obtained in this case, lumbar puncture is always recommended. Care must be taken in doing the puncture to avoid trauma, particularly when done in the first forty-eight hours, and for this reason, I practice giving a few drops of chloroform and use a small Luer hypodermic needle. When bloody fluid is obtained, the child

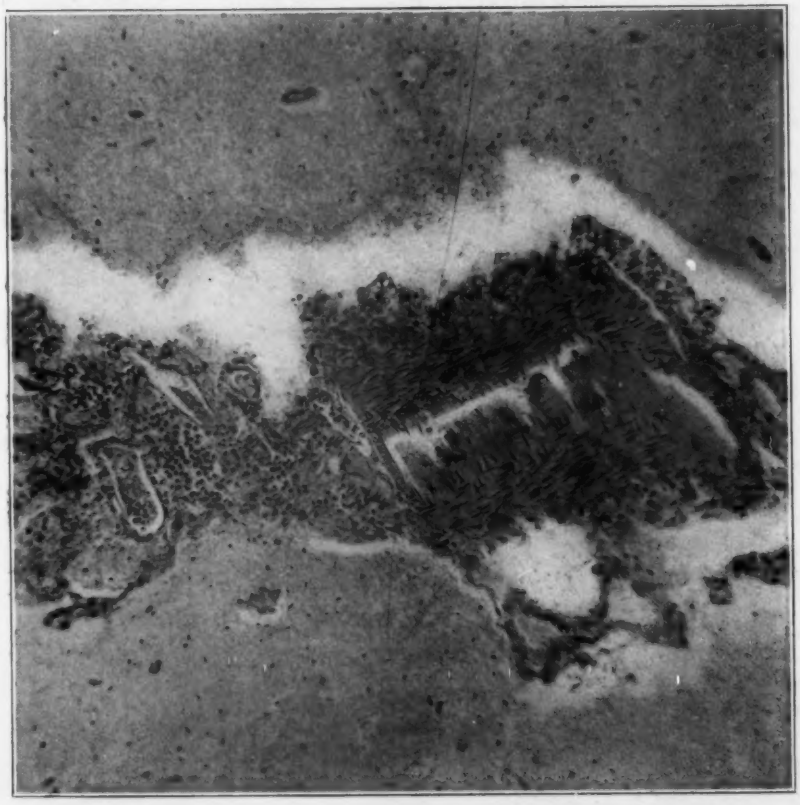

Fig. 28 (case 12).—Pia-arachnoid deep in a sulcus on the undrained side showing fibrous tissue and cell infiltration.

is generally better after the first or second puncture, but I make repeated punctures even in the absence of symptoms until the fluid is entirely clear. The intervals between punctures depend on the severity of the symptoms (being shorter in severe cases) and the amount of blood present. It is recognized that a new-born child with some blood in the cerebrospinal fluid will recover spontaneously, but when the blood has produced symptoms, the normal recuperative powers should be aided by repeated punctures.

Fortunately, the greater number of hemorrhages at birth, excluding those desperate cases in which there are massive hemorrhages, fall into this group.

Major operative procedures are recommended only in selected cases because of the high mortality which discourages all effort, resulting in the attitude, still too frequently encountered, that a child with a hemorrhage is so likely to be a defective that it is better for it to go

Fig. 29 (case 12).—Pia-arachnoid deep in a sulcus on the drained side in marked contrast to that shown in figure 28 corresponding to the gross changes in figures 24 and 25.

untreated with the hope that it will succumb. This is unfair in that it does not give the child a chance, and especially because many of the untreated survive with a poor chance for normal cerebral development. A good example of this was seen in a child who had had severe convulsions immediately after birth. The diagnosis of cerebral hemorrhage was made, and there was a stormy course for a month, during which time little hope of recovery was maintained. After a few weeks the

child had apparently recovered, but at the age of 3½ years, a general convulsive seizure was followed by other seizures at intervals of a few months.

General muscle rigidity is a prominent sign in neglected cases and usually starts when the acute signs of cerebral irritation cease.

CASE 14.—*Cerebral irritation when a few days old. Muscular rigidity at 1 month, which increased until treatment, lumbar puncture, was instituted at age of 2 months. Condition satisfactory when child was 6 months old.*

Baby P. Z., when a few days old had had a seizure, with marked cyanosis. When the child was 2 weeks old the mother noticed postcervical rigidity. At the age of 1 month there was general rigidity, and the head was drawn back to such an extent that the child could not lie in the dorsal position and could be raised from a lying to a sitting position by lifting the head (fig. 30). Because the eyes were rolled upward and did not follow an object, the mother also feared he could not see. Repeated lumbar punctures, fourteen in all, over a period of four months, were followed by satisfactory disappearance of the rigidity.

Fig. 30 (case 14).—The postcervical rigidity permitted the child to be raised to a sitting position by lifting the head (illustration taken from a moving picture film).

From this time, the mental and physical condition of the child did not cause concern. The photograph (fig. 31) was made when the child was 1 year of age to show normal muscle control.

The history of cerebral irritation during the first few days of life and the fact that improvement follows lumbar punctures differentiates these patients from the large group of children with spasticity resulting from developmental defects.

One child came under observation at the age of 9 years. This child with her twin had had a normal birth, and at the age of 4 weeks was examined by the pediatrician, who told the mother that the patient was the better of the twins because of her ability to hold her head and spine erect. This probably indicated the early rigidity of a chronic meningitis; the mental and physical development of the patient, not so good as that

of the other twin, merged into a state of epilepsy at the age of 9 years. The head of the child had the appearance of a slight degree of hydrocephalus, and this fact was borne out by the roentgenogram of the air filled ventricles.

In a few cases, lumbar puncture will not control the symptoms, and a more complete and thorough drainage must be established through a decompression or osteoplastic flap.

CASE 15.—*Cerebral irritation at age of 1 week. After repeated lumbar punctures, all symptoms disappeared, except muscular rigidity, which improved during a period of subtemporal drainage but returned when drainage ceased. An osteoplastic bone flap followed by drainage entirely relieved the condition.*

Fig. 31 (case 14).—Normal muscle control when a little more than 1 year old (illustration taken from a moving picture film).

E. S., had had a convulsion on the seventh day after birth, and there was bulging of the fontanel. Lumbar puncture revealed blood-stained cerebrospinal fluid, diminished the bulging of the fontanel, and the convulsions ceased. Repeated punctures, six in all, until the age of 6 weeks, improved only temporarily the state of rigidity and the tension of the fontanel. At this stage, a more radical procedure was deemed necessary; an opening was made in the right subtemporal region, and a small rubber tissue drain was inserted. As long as drainage of cerebrospinal fluid continued, the condition of the child was satisfactory, but soon after the drain was removed, on the ninth day after operation, the tension and rigidity returned. The mother expressed anxiety over the condition of the child as compared with her two other normal children at this age. On the seventy-second day after birth, a right osteoplastic bone flap was done with the

hope of draining more thoroughly the subarachnoid space. When the pia-arachnoid overlying the hemisphere was exposed, a low grade meningitis similar to that seen in the dogs was found. Drains were inserted over the cortex, and the dura was closed loosely. The rigidity gradually diminished and disappeared. The fear of the mother that the child would be backward, entirely subsided as normal mental and physical development (fig. 32) progressed throughout the first months after the operation. The child is now 4 years old and is quite like her brother and sister.

Fig. 32 (case 15).—Patient at the age of about 16 months showing an active, alert child.

Six of the twenty-six puppies injected had a rather marked degree of ventricle dilatation associated with chronic meningeal thickening and cortical scarring. The dilatation did not progress to an extreme degree and was associated with an excess of fluid over the cortex, which leads to the belief that the cerebrospinal fluid blocking was due to interference of absorption rather than to a blocking at the basal foraminae.

The two following cases in which the patients had slight enlargement of the ventricle and a large amount of fluid over the cortex with clinical evidence of hydrocephalus are of this type, although the cerebrospinal fluid blockage is different from that seen in case 1.

CASE 16.—*Cerebral trauma at the age of 2 months. Indefinite cerebral symptoms with gradual enlargement of the head until 8 months of age when examination showed slight enlargement of the ventricles and a large amount of fluid over the cerebral cortex.*

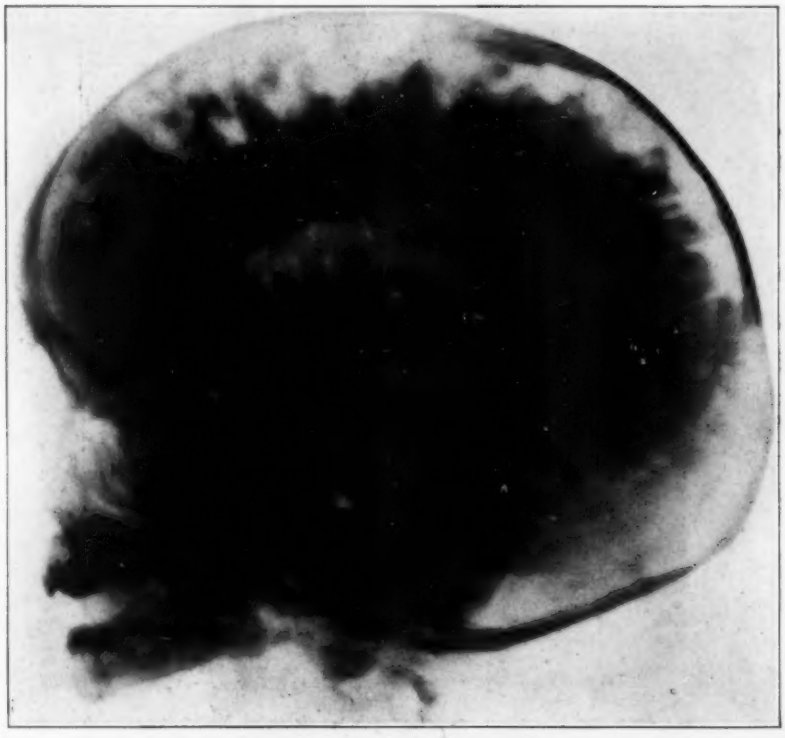

Fig. 33 (case 16).—Large amount of air over the cerebral cortex with only slight dilatation of the cerebral ventricles. The air was introduced through a lumbar puncture needle after the withdrawal of a large amount of fluid.

Baby W. W., fell from his crib at the age of 2 months. Little attention was paid to the injury, but during the following weeks the child was listless and inactive. At the age of 8 months, he was unable to hold up his head. When examined by me at the age of 9 months, the circumference of the head was 45.5 cm., the sutures were separated, and the fontanel was large and tense, giving the child a typical hydrocephalic appearance. A large amount of cerebrospinal fluid was withdrawn through a lumbar puncture needle, and air was injected (figs. 33 and 34). The illustrations show a large amount of air over the cerebral cortex with only slight dilatation of the ventricles. Repeated lumbar punctures failed to control the symptoms. Because of the long duration and the

advanced stage of the condition, so little was promised the parents that they declined operation. The child is now 2½ years old and is entirely helpless.

CASE 17.—*Small amount of blood in the cerebrospinal fluid at birth. Early cerebral irritative symptoms and during the third month evidence of hydrocephalus. Ventricles only slightly enlarged but a large amount of fluid over the cerebral cortex. Condition corrected by osteoplastic bone flap with free drainage of cerebrospinal fluid on one side and decompression with free drainage on the other side.*

Fig. 34 (case 16).—Anteroposterior view also showing a large amount of air over the cerebral cortex with wide sulci.

Baby V. D., was delivered with high forceps after slow labor. Immediately after delivery, the condition was satisfactory. Later in the day, there was slight twitching of the hands and feet with some cyanosis. For the next forty-eight hours the child cried a great deal and refused to nurse, and its temperature ranged as high as 103 F. Lumbar puncture on the third day revealed cerebrospinal fluid with a pale yellow tinge. Because of the mild degree of twitching and the fact that the fluid was yellow on the third day, a favorable prognosis was given, as

it was believed the small amount of blood would be absorbed. Another puncture was advised to check the condition of the cerebrospinal fluid before the mother and the baby were discharged from the hospital. On the seventeenth day after birth, I examined the child again; the circumference of the head was 39 cm., the veins of the scalp were dilated, especially those from the bregma over the frontal region, the fontanel was tense, and the sutures were separated. Lumbar puncture revealed a more deeply yellow-tinged cerebrospinal fluid than at the time of the puncture two weeks previously. Three days later, the circumference of the head had increased 5 mm., and the cerebrospinal fluid pressure was 180 mm. of water. The appearance of the child was now definitely that of one with a

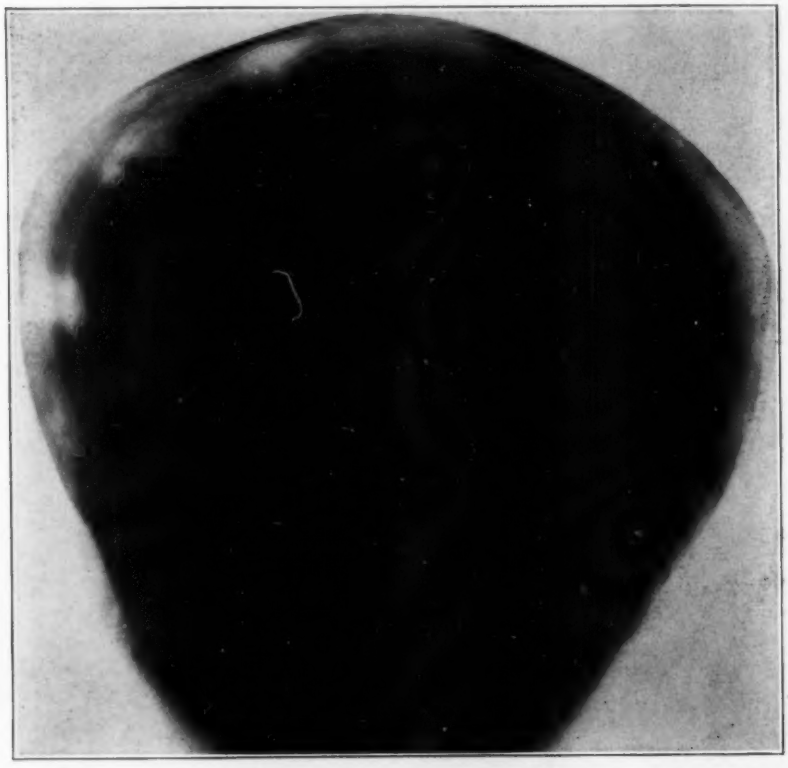

Fig. 35 (case 17).—Air injected through a lumbar puncture needle after the withdrawal of cerebrospinal fluid is shown in the wide sulci and over the cortex. The ventricles not shown in the print were slightly dilated.

beginning hydrocephalus, and it was determined to perform punctures at short intervals. Twelve additional punctures at intervals of from two to five days were made. When the child was 7 weeks old, air was introduced through a lumbar puncture needle, and the roentgenogram showed wide sulci, an abnormally large space between the cortex and the dura and a slight enlargement of the ventricles indicating an excessive amount of cerebrospinal fluid (fig. 35). At the age of 9 weeks, in spite of the lumbar punctures, the circumference of the head was 42 cm., the fontanel was larger, the sutures were separated, the

veins of the scalp dilated, and the head was heavy, requiring support when the child was picked up.

At this time, an osteoplastic bone flap was made uncovering a large part of the right cerebral hemisphere. The pia-arachnoid was definitely thickened. The cortical veins were engorged, and the arachnoid over the sylvian fissure and the sulci was literally distended with fluid. When the membrane over the sylvian fissure was punctured, fluid slowly escaped as though seeping from a mesh. The wound was closed with a drain. For several days after the operation, there was free drainage of cerebrospinal fluid. Three weeks after operation, the circumference of the head was 41.5 cm., the fontanel was soft, scalp veins were not overfilled, and the child had regained some control of the muscles of the neck but was still unable to hold the head erect. The condition continued to improve for several weeks, when the tension was again increased and the head began to enlarge. Frequent lumbar punctures were tried, but failed to control the condition, and at the age of 19 weeks an opening was made in the left temporal region and drains were inserted. From this time on, the fontanel gradually decreased in size and the circumference increased only at the normal rate. The condition of the child at the age of 13 months is shown in figures 36 and 37. Except for slight enlargement of the head, the physical and mental condition is entirely normal.

Fig. 36 (case 17).—Photograph of patient at the age of 13 months. The head is larger than normal, but the sutures are closed, and there is no evidence of increased intracranial tension.

The clinical course in this case, different from that of the other groups described, typifies what happens infrequently, but which I believe is nevertheless a definite clinical entity. Through the irritating effects of the blood in the cerebrospinal fluid, there is interference with the

absorption of the fluid. Puncture of the dura as by lumbar puncture in the milder cases or by an extensive opening as a bone flap in the more severe types unblocks at some point, and absorption is reestablished.

That the opening of the dura has an influence on this type of case was first brought to my attention in a child born after a prolonged and difficult labor, who was normal for a period of two weeks, after which

Fig. 37 (case 17).—Lateral view of the head at the age of 13 months.

there was rapid enlargement of the head. It was thought that there was a blood clot over the cerebral cortex, and several small openings were made through the skull and dura. A clot was not found, and the wounds were closed tightly. From the time of the operation, the head ceased to enlarge. An explanation of this was not had at the time, but I now believe that the mere opening of the dura helped rid

the subarachnoid space of the irritating cerebrospinal fluid. This child is now 13 years of age, has always been backward, and since the age of 5 years, has had convulsive seizures. Early complete subarachnoid drainage, would perhaps, have given this child a much better chance.

Fig. 38 (case 18).—Meningeal thickening twenty days after cerebral trauma with bloody cerebrospinal fluid.

In 1903, Dr. William G. Spiller [4] called attention to the importance of cases of cerebral trauma without displacement of bone in which a blood clot, even though small, is present, and in spite of the early disap-

4. Spiller, W. G.: Traumatic Lesions of the Brain in Their Relation to Operation, Internat. Clin. **4**:102, 1923.

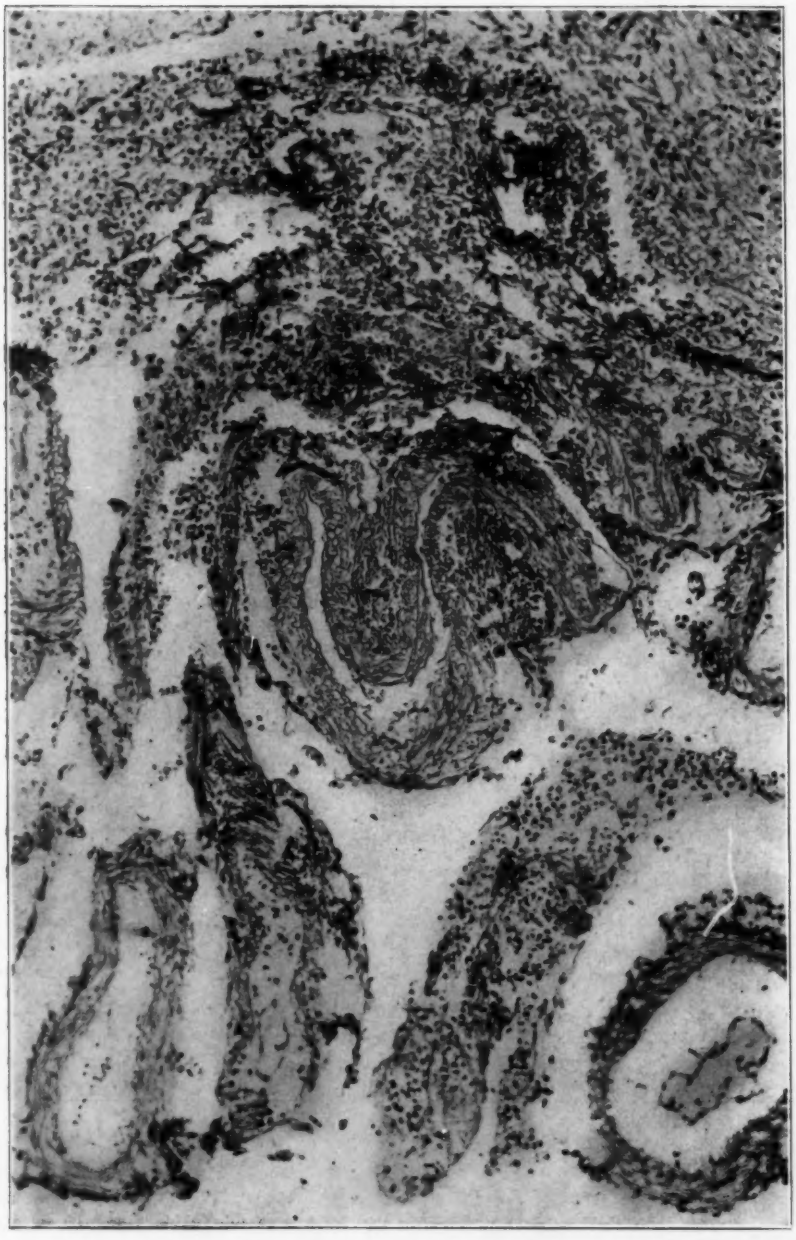

Fig. 39 (case 18).—Section of the meninges from the base showing meningeal thickening and cell infiltration.

pearance of symptoms of compression, the patient is in danger of becoming epileptic or developing traumatic insanity.

In 1904, Dr. Adolf Meyer [5] in his discussion of mental patients who had previously had a cerebral trauma remarked: "Whether the cranium is fractured or not means relatively little. It would seem, however, that for chances concerning life, a relatively extensive destruction of the skull is rather more favorable than otherwise."

In the light of my experimental work the drainage of cerebrospinal fluid seems to be of paramount importance, and I am inclined to feel that the danger of immediate and late symptoms is lessened in the compound cases in which the dura is opened allowing a free escape of blood and cerebrospinal fluid.

Dr. Harvey Cushing,[6] in his paper in 1907, calls attention to the advisability of decompression and drainage. This marks the beginning of a type of cranial surgery which has proved very useful. Confusion in the selection of patients for operation occurs because of failure of surgeons to consider carefully the underlying lesion in attempting to determine whether the patient should or should not be treated by decompression. For instance, in some clinics, an attempt has been made to settle the question by operating on a given number of consecutive "fractured skulls" and comparing them with a second series, none of which were subjected to operation. The outcome of these discussions has resulted in the conviction that there is a type of case in which the patient may recover spontaneously, but the recovery can be speeded and a more simple postoperative course can be assured by drainage of cerebrospinal fluid. It has further been recognized that in many of these cases the bloody cerebrospinal fluid can be drained through repeated lumbar punctures, thus avoiding the more radical procedure of decompression and drainage. Here again the pendulum may swing too far, and care must be taken not to overlook the case in which lumbar puncture will not suffice and a decompression or even a bone flap is required.

The importance of bloody cerebrospinal fluid as a result of injuries without displacement of bone is shown in the following fatal case in which the symptoms immediately after the injury were slight. During the second week, meningeal irritative signs gradually developed to a serious stage, and the patient died during the third week in spite of lumbar puncture and late decompression.

CASE 18.—*Late appearance of symptoms following the escape of blood in the cerebrospinal fluid. Decompression delayed until the sixteenth day after the*

5. Meyer, A.: The Anatomical Facts and Clinical Varieties of Traumatic Insanity, Am. J. Insan. **60**:373, 1904.

6. Cushing, A.: A Discussion of some Immediate and some Remote Consequences of Cranial Injuries, Based on Three Clinical Histories Which Illustrate the Extradural, Subcortical, and Intermeningeal Types of Intracranial Hemorrhage, New York M. J. **85**:214, 1907.

accident accomplished nothing. Section of the meninges showed marked meningeal reaction.

G. G., a man, aged 35, was thrown from an automobile and struck his head. He went to his home, and his condition did not cause any concern until the end of the first week, when there was headache and mental confusion with slight elevation in temperature. He was treated at home for several days, during which time the symptoms increased. When the patient was admitted to the hospital fourteen days after the accident, the pulse rate was 60 per minute, there was postcervical rigidity, a positive Kernig sign, some delirium, severe headache and beginning choking of the disks. Lumbar puncture showed yellow-tinged cerebrospinal fluid. Following the puncture, the patient was more comfortable. A second lumbar puncture was made after an interval of six hours, and a third, twenty-four hours later. The symptoms increased, and a right subtemporal decompression was performed forty-eight hours after admission, at which time the patient presented the appearance of one suffering from advanced meningitis. When the dura was opened, there was bulging of the cortex and only a small amount of cerebrospinal fluid escaped, indicating that the condition had reached the stage of cerebral edema. The pia-arachnoid was opaque, but there was no evidence of exudate. Drains were inserted over the cortex. Following the operation, there was scant drainage of cerebrospinal fluid, and the condition grew worse until death four days later. Autopsy revealed a film of blood mixed with cerebrospinal fluid throughout the subarachnoid space. The meninges at the base were thickened (fig. 38) and blood-stained. A section of the meninges from this area (fig. 39) showed the reaction.

In this case, the disturbance at the time of admission to the hospital is now believed to have been due to edema of the brain which, no doubt, followed a stage in which there was an excess of fluid in the subarachnoid space. The period for lumbar puncture had passed, and a more radical procedure for complete drainage was indicated.

In the following case, lumbar puncture was not made, as there was evidence of "medullary disturbance." On the fourth day, a convulsive seizure occurred, and because of the serious condition following it, a right subtemporal decompression was performed.

CASE 19.—*Cerebral trauma with a general convulsive seizure and complete loss of consciousness on the fourth day.*

J. G. N., a married woman, aged 40, was injured in an automobile accident, receiving a blow in the right frontal region. She was admitted to the hospital one hour later, when there was some bleeding from the nose and right external auditory canal; the blood was not mixed with the cerebrospinal fluid. In the beginning she was unconscious; this condition improved, but mental confusion continued. In spite of evidence of "medullary disturbance" with marked increase in the deep reflexes, clonus and a bilateral Babinski sign, the condition did not seem alarming until the afternoon of the fourth day, when she had a convulsive seizure with cyanosis, a severe drop in the blood pressure, pulse and respiratory rate, the latter reaching 10 per minute. Following the seizure, there was complete loss of consciousness for four hours, at which time a right subtemporal decompression and free drainage of cerebrospinal fluid were accomplished. Following the operation there was prompt recovery, and the patient was discharged on the twelfth day, at which time there was some blurring of vision and slight mental confusion. When examined recently two and a half years after the accident, the patient was normal.

The sudden onset of symptoms in a man four days after an accident is shown in the following patient:

CASE 20.—*Cerebral irritation with bloody fluid four days after trauma promptly relieved by lumbar puncture.*

J. S., a man, aged 34, was admitted to the hospital immediately after an injury in the right frontal region of the head. There was little headache, and the temperature ranged from normal to 100 and the pulse rate from 70 to 100 per minute for the first four days. During the evening of the fourth day, the patient complained of severe neuralgia-like headache; he vomited, and the temperature registered 97 F. with a fall in pulse rate to 60 per minute. Lumbar puncture revealed bloody cerebrospinal fluid. Later, lumbar puncture showed the cerebrospinal fluid gradually returning to normal, and all symptoms disappeared.

The symptoms in this patient were due to a gradually increasing meningitis. It is unwise to disturb a patient who is apparently doing well, but an early lumbar puncture would have prevented the severe reaction in this case. One year after the accident this patient had indefinite symptoms, such as headache and dizziness of a mild degree.

The late appearance of signs and symptoms is shown in the following case:

CASE 21.—*Cerebral trauma with bloody cerebrospinal fluid. Gradually increasing symptoms for two weeks; gradual disappearance of symptoms following repeated lumbar puncture.*

W. C., a man, aged 20, received a severe blow over the right frontal region of the head while playing football. After a few moments he continued playing, and in spite of a slight headache, worked the following day and attended a dance during the evening. He complained slightly, and forty-eight hours after the injury consulted his family physician because of mild headache and occasional vomiting. Two weeks after the date of the injury, I saw him because the pulse rate was ranging from 48 to 52 per minute. He was rather dull when left alone, but when stimulated, would talk and seemed entirely normal. He said there was no real headache, but a feeling of tightness and some tenderness of the scalp. The examination showed a rather listless youth with speech distinct but slow. The disks showed definite changes from the normal, with a mild degree of choking. Three hours after the puncture, the patient said he felt different. The dull feeling in the head was gone, and he was more alert. Lumbar puncture twenty-four hours later showed the same yellow fluid. Two weeks after the first puncture, the fluid was almost entirely clear. Twenty-six days after the first puncture, because of nervousness, another puncture was made and the fluid was colorless. The patient did not complain of headache, and returned to his work.

CASE 22.—*Cerebral trauma with symptoms two weeks later, but patient not treated until one month after the accident. Well marked meningeal reaction with evidence of increased intracranial pressure, relieved by decompression and drainage.*

R. S., a boy, aged 12, fell from a fence and struck his head in the left parietal region. There was nausea and vomiting and some headache for two days. After that time he seemed normal, but later developed an internal squint of the right eye and complained of photophobia. He played normally for two weeks, when there was some drowsiness, and he was inactive for the greater part of the next two weeks. When examined four weeks after the accident, there was marked choking of the disk, paralysis of the right external rectus and stupor, but he could

be aroused to carry out simple commands. The pulse rate was 60 per minute, the leukocytes numbered 11,000, and a suggestive Kernig sign was present. The roentgenogram showed a linear fracture of the right parietal region. A right subtemporal decompression was performed, and drains were inserted. The dura was tense, and when opened there was free drainage of cerebrospinal fluid. The following day, the external rectus muscle was less weak. All symptoms gradually disappeared during a period of three weeks, when the patient was discharged.

CASE 23.—*Cerebral trauma with delay of serious symptoms for seven weeks. Late appearance of convulsions and partial hemiplegia at first led to the diagnosis of apoplexy. Because of history of trauma, decompression with drainage was done.*

F. S., a man, aged 55, fell on his head while climbing an ice-covered wooden fence. He was at first dazed, but walked home. Three weeks later, he had vague symptoms for which he consulted a physician. Seven weeks after the accident, he returned home after attending church, walked upstairs to retire for the night and had a convulsive seizure, after which there was headache and vomiting, slight weakness of the right side of the face and of the arm and mental confusion. The symptoms continued, and I first saw him four days later. Examination at that time revealed the patient in stupor; the pulse rate was slower than normal, there was a mild choking of the disks and slight weakness of the right side of the face and of the right arm. With the history of the sudden onset four days before, the diagnosis of cerebral hemorrhage was made. In discussing the case with the patient's wife following the consultation, she remarked that the patient had never been the same since he fell over the fence. This was the first mention of the accident, which, because of the interval of seven weeks, had not been thought to have any connection with the present condition, and was not mentioned by the other members of the family who had originally given the history. Careful questioning revealed that the patient had had vague symptoms and had consulted a physician for slight headache three weeks after the accident. It was then concluded that the symptoms were, perhaps, due to the accident, and exploration was advised. During the period of twenty-four hours in the hospital before the operation, the temperature ranged from 100 to 101 F., and the pulse rate from 45 to 65 per minute. There was beginning choking of the disks, weakness of the muscles of the right side of the body and stupor. Decompression was performed and an opaque arachnoid with distention of the cortical vessels was seen. A drain was placed beneath the dura and the wound was closed. Following the operation, there was a gradual falling of the temperature, which reached normal on the eighth day after admission. All symptoms improved, and the patient was discharged from the hospital on the thirty-third day. Ten years have passed since the operation, and the patient is living and well.

Just what part syphilis plays in spontaneous cortical hemorrhages with extravasation of blood into the cerebrospinal fluid has been variously stated.

CASE 24.—*Cerebral syphilis with a sudden hemorrhage into the cerebrospinal fluid followed by severe pain and delirium. Gradual improvement of symptoms for five days. Lumbar puncture on the fifth day showed yellow fluid. Rapid improvement following lumbar puncture.*

G. J., a married man, aged 37, while driving his car on April 27, 1923, was suddenly seized with severe headache and vomiting. He was taken to the office of a physician in a state of collapse. For one week following the onset of symptoms, he was wildly delirious. There was elevation in temperature, and the pulse rate was rapid. He was admitted to the hospital five days after the attack,

complaining of headache and pain in the extremities. Lumbar puncture made the next day revealed slightly bloody cerebrospinal fluid; another a week later showed clear yellow cerebrospinal fluid. The patient was discharged from the hospital eleven days after admission, the stupor following his delirium having cleared up. The Wassermann reaction of the blood and cerebrospinal fluid was positive, and the patient was treated for syphilis. It is now almost five years since his discharge from the hospital, and there has not been any recurrence of the symptoms. The symptoms in this type of case are due to meningeal irritation. The fact that this patient had syphilis and had refused thorough treatment was known to his physician; he, therefore, attributed the mental upset to this, and was planning to have the patient committed to an institution. As the condition improved after five days, the patient was admitted to a general hospital, where it was decided the mental condition was due to the blood in the cerebrospinal fluid.

Arteriosclerosis and hypertension play an important rôle, and care must be taken to differentiate cases in which the symptoms are due to escape of blood into the cerebrospinal fluid from those due to a hopeless subcortical clot. The first intimation of the hopeful type is found when the patient shows evidence of meningeal irritation ranging from severe headache and postcervical pain to rigidity and convulsive seizures with elevations in temperature and pulse rate. In either type there must be some blood in the cerebrospinal fluid; but a lumbar puncture with the withdrawal of even a small amount of fluid will cause improvement in patients with the simple type and will have a bad influence if any on patients with subcortical clot.

CASE 25.—*Cerebral arteriosclerosis with bloody cerebrospinal fluid and severe cerebral irritative symptoms which were relieved by repeated lumbar punctures.*

J. H. S., a married man, aged 54, after hurriedly driving his car, became slightly confused mentally and thick in his speech. There was a slowly increasing stupor, which was never deep. Two hours after the onset, the patient had a general convulsive seizure; during the next ten hours, he had three more, at which time there was slight weakness of the right side of the face and of the right arm. The blood pressure was 200 systolic and 130 diastolic and later dropped to 190 systolic and 90 diastolic. When I examined the patient the first time, at 4 p. m., the following day, twenty hours after the onset of the trouble, there was partial aphasia and slight weakness of the right arm and of the right side of the face, and the reflexes were greater in the right than in the left upper extremity. There was stupor and mental confusion. The patient seemed to be uncomfortable because of headache. On lumbar puncture, bloody cerebrospinal fluid was withdrawn. Following the puncture, the patient was more comfortable. Repeated punctures were made until the fluid was clear one week after the onset, and the patient gradually improved, though the aphasia never entirely cleared up. The patient is still living, two and one half years later, the blood pressure has remained high, and he now presents the usual picture of cerebral arteriosclerosis.

CASE 26.—*Bloody cerebrospinal fluid perhaps due to rupture of an arteriosclerotic cerebral vessel. On admission of patient to hospital one week after sudden onset, the signs and symptoms suggested tumor of the brain. Repeated lumbar punctures followed by disappearance of all signs and symptoms.*

Mrs. C. G., aged 56, was suddenly seized with severe pain in the head. Within twenty-four hours the patient was in coma which lasted for several hours. Severe headache with paroxysmal attacks of agonizing pain and loss of consciousness

occurred several times daily. When admitted to the hospital one week after the onset, she showed bilateral choked disks, bilateral abducens weakness and slight weakness of the left side of the body, including the face. There was postcervical rigidity and positive Kernig sign. Dizziness was troublesome, especially when the position was changed. The diagnosis of cerebellar tumor was made, but because of the sudden onset, postcervical rigidity, positive Kernig sign, and slight elevation in temperature and increased pulse rate, the immediate cause of the symptoms was believed to be due to the escape of blood in the cerebrospinal fluid. A lumbar puncture was made, and bloody cerebrospinal fluid was obtained. The condition was followed by immediate temporary improvement in the symptoms. Repeated lumbar punctures, nine in all, brought about a subsidence of symptoms, though the disturbance of the eye movements persisted for three months. Convalescence was slow, but the patient is living and well and free from symptoms with a blood pressure of 160 fifteen months after the illness.

Lumbar puncture in the presence of choked disk due to tumor is an extremely dangerous procedure; on the other hand, when there is an excess of cerebrospinal fluid, a lumber puncture is not dangerous but offers relief. In this case, the possibility of tumor as the underlying cause of the blood must be considered, but there can be no doubt as to the blood having caused the immediate symptoms, and the interval of one year without symptoms makes the diagnosis of tumor unlikely. A similar case recently came under observation.

CASE 27.—*Bloody cerebrospinal fluid with increased intracranial pressure and other signs suggesting tumor of the brain. Gradual improvement of symptoms as lumbar punctures were made.*

C. C., a married man, aged 46, while at work was suddenly seized with severe pains in the head and was immediately taken to the hospital in an unconscious condition. There was postcervical rigidity and a positive Kernig sign. When he was examined, twenty-four hours after the onset of the trouble, the pulse was slow and the disks indicated an increase in intracranial pressure. Lumbar puncture revealed a bloody cerebrospinal fluid. In this case, the early change in the disk and the slow pulse rate with slow clearing up of the symptoms after puncture made one suspicious of something more than a little blood mixed with the cerebrospinal fluid, perhaps a tumor or large hemorrhage with some leakage into the subarachnoid space. Three weeks after the onset of the symptoms, the fluid was almost entirely clear; the patient was still somewhat confused, but gradually improved, following much the same course as that noted in case 24. It is now three months since the onset, and the patient is gradually improving; all signs and symptoms have disappeared, except dizziness and some unsteadiness of gait.

SUMMARY

Short clinical histories of twenty-seven patients with bloody cerebrospinal fluid are presented. In most of the cases, the blood in the fluid resulted from trauma, and the effect of the blood is shown in the acute, subacute and chronic stages.

In two cases, the blood was due to congenital venous anomalies, and in one case to a tumor of the brain present at the time of birth.

Five patients ranging in age from 12 to 44 years had aneurysms of the anterior cerebral arteries.

In four of the patients who recovered, the exact underlying causes could not be determined, but arteriosclerosis was the most probable factor.

COMMENT

The material has been collected for the purpose of demonstrating the acute and chronic changes in the central nervous system following the introduction of blood in the cerebrospinal fluid.

Cases in which there were meningeal irritations due to a free mixture of the blood with the fluid have been selected, and the discussion does not include cases in which the patients had large blood clots.

The symptoms immediately following the escape of blood into the cerebrospinal fluid depend on the amount of blood and vary from slight headache to severe pain with convulsive seizures and loss of consciousness. The most important signs and symptoms in patients with a small quantity of blood usually appear after an interval of a few days and are due to the reaction of the meninges. This state is characterized by headache of a neuralgic type, delirium, mild elevation in temperature, slight increase in pulse rate, postcervical rigidity and a positive Kernig sign. These symptoms may gradually subside as the blood is absorbed. In adults, complete recovery may take place, but infants presenting the early symptoms, if allowed to go untreated, frequently develop rigidity of the muscles and epilepsy. If the early symptoms progress, the signs of cerebral edema with evidence of marked increase of intracranial pressure may appear and may result in death.

An analysis of the signs and symptoms due to bloody cerebrospinal fluid impresses one with the importance of recognizing the condition, because the diagnosis in these patients may be confused with that in almost any of the common lesions of the brain from meningitis to tumor of the brain. In some cases, the disturbance due to the blood in the cerebrospinal fluid must be cleared up before the primary lesion can be diagnosed.

Treatment depends on the stage of the disease and should be carried out with the view of removing the irritating blood and preventing or relieving the meningitis. Absorption of some blood always takes place, but this is associated with meningeal thickening which may cause a block in the channels through which the fluid is returned to the blood stream. Treatment, therefore, has to do with the drainage of fluid which may be accomplished through lumbar puncture or the more radical procedure of decompression or even a bone flap. Some of the cases for this paper have been selected for the purpose of showing types suitable for the various procedures.

This work has been carried on under the direction of Dr. Adolph Meyer. Dr. Robert B. Wright assisted in the study of the specimens and Miss Cecelia Bisson made the illustrations.

BILATERAL LOBAR ATELECTASIS

REPORT OF A CASE WITH AUTOPSY OBSERVATIONS *

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This is a report of a case in which bilateral lobar atelectasis was associated with acute pancreatitis (fat necrosis). The observations made at autopsy suggest a probable explanation for the collapse of the lower lobes of the lungs.

REPORT OF A CASE

A woman, aged 48, who had enjoyed good health until October, 1925, developed symptoms of hyperthyroidism. A thyroidectomy was performed on Nov. 28, 1925. The gland showed slight hyperplasia. Preceding the operation, the basal metabolic rate was plus 56 per cent. In March, 1926, the basal metabolic rate was minus 21 per cent, and the patient showed other signs of hypothyroidism including obesity. After this time, thyroid extract was administered regularly.

Four months before her final admission to the hospital, the patient had intermittent colicky pains in the upper right quadrant of the abdomen, which were diagnosed as "gallbladder attacks." Three days before admission (Dec. 4, 1927), the patient had a severe persistent pain in the upper right quadrant of the abdomen, which became localized in the region of the gallbladder and was accompanied by vomiting. The pain was referred to the back and was described by the patient as being "between the shoulder blades." On December 7, the patient had a transient cyanosis which lasted for fifteen minutes and was characterized by rapid respiration and a feeling of impending danger.

On admission to the hospital, on December 8, the patient had a temperature of 38 C.; the pulse rate was 130 and the respiratory rate was 25. Physical examination revealed tenderness in the region of the gallbladder and a questionable tumor-like mass which appeared to be an empyema of the gallbladder. The lower lobe of the right lung was thought to be consolidated, and over the lower lobe of the left lung were heard numerous moist râles and tubular breathing. A diagnosis was made of empyema of the gallbladder with possibly bronchial pneumonia. Because of the serious condition of the patient, an exploratory operation was postponed.

The average white blood cell count while the patient was in the hospital was 16,000 per cubic millimeter. The red blood cell count was 3,400,000. Eighty-three per cent of the white blood cells were polymorphonuclear neutrophils. The urine was acid in reaction; the specific gravity was 10.10, and all specimens showed two plus albumin. There was no glycosuria and the microscopic examinations showed the constant presence of a few pus cells. A liver function test showed 1.2 mg. serum bilirubin. The blood sugar averaged 120 mg. per hundred cubic centimeters. Plasma carbon dioxide was 39 and the blood urea, 57. A culture of the sputum did not reveal pneumococci. A roentgenogram was reported as unsatisfactory (fig. 1), but because the patient was thought to have pneumonia there was some objection to making another roentgenogram.

On December 21, the abdominal tenderness became more generalized, and the abdomen appeared to be more distended than before. An exploratory

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laparotomy was therefore performed on the patient without removing her from her bed. The operation was done under local anesthesia with procaine hydrochloride together with nitrous oxid-oxygen analgesia. An upper right rectus abdominal incision was made, and the peritoneal cavity was then exposed. The liver was found to be pushed over to the right and numerous adhesions between the anterior abdominal wall and the region of the falciform ligament were found. Many small, dull white, oval areas were scattered throughout the peritoneal cavity; these were more numerous on the omentum, a condition which is typical of fat necrosis. The lesser peritoneal cavity was distended with a pale red, serous fluid. An opening was made in order to drain the fluid, and a drain was placed in the region of the pancreas. Eight hours later, the patient ceased to breathe.

Necropsy Report.—An autopsy performed one hour post mortem revealed the following: The peritoneal cavity contained blood-stained serum and a blood

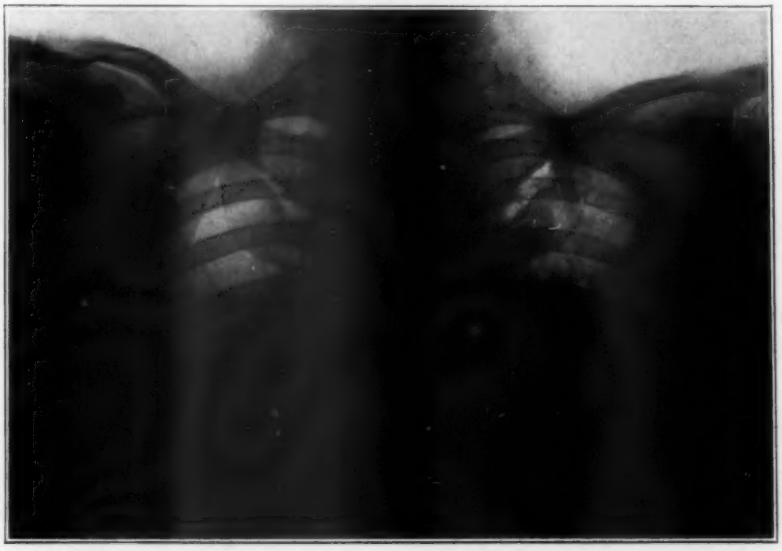

Fig. 1.—Bilateral lobar atelectasis; consolidation of the lower lobes.

clot. The falciform ligament was 4 cm. to the right of the midsternal line; the greater omentum was uniformly distributed over the intestines with the lower border at the pelvis. Numerous oval, dull white, discrete areas averaging 10 mm. in diameter were scattered throughout the omentum and peritoneal cavity; the tissue surrounding these areas was not discolored. On account of edema and of infiltration of the tissue surrounding the foramen of Winslow which produced mechanical obstruction between the two peritoneal cavities, the lesser peritoneal cavity did not communicate with the greater cavity. The lesser cavity contained about 3,300 cc. of blood-stained serous fluid in which were floating bits of debris.

When the sternum with the attaching costal cartilages was removed, the mediastinum was found in the midline. Both pleural cavities were clean. The dome of the diaphragm on the right was at the level of fourth rib, and on the left, at the level of the fourth intercostal space.

The pericardial cavity was clean. The apex of the heart was 10 cm. to the left of the midsternal line and at the fifth rib.

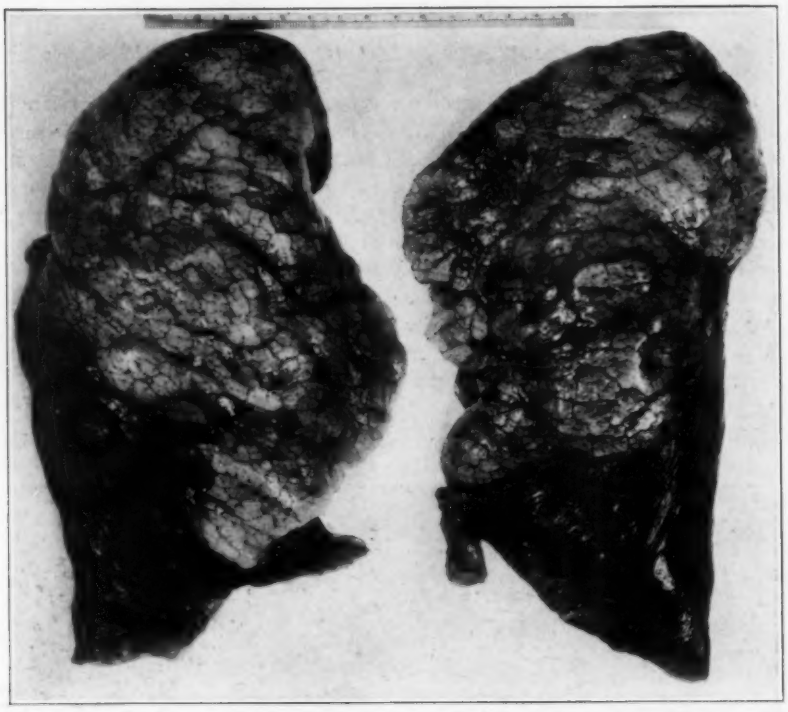

Fig. 2.—Lungs in case of bilateral lobar atelectasis. Note the relatively small lower lobes and the sharp line of demarcation of the atelectatic areas.

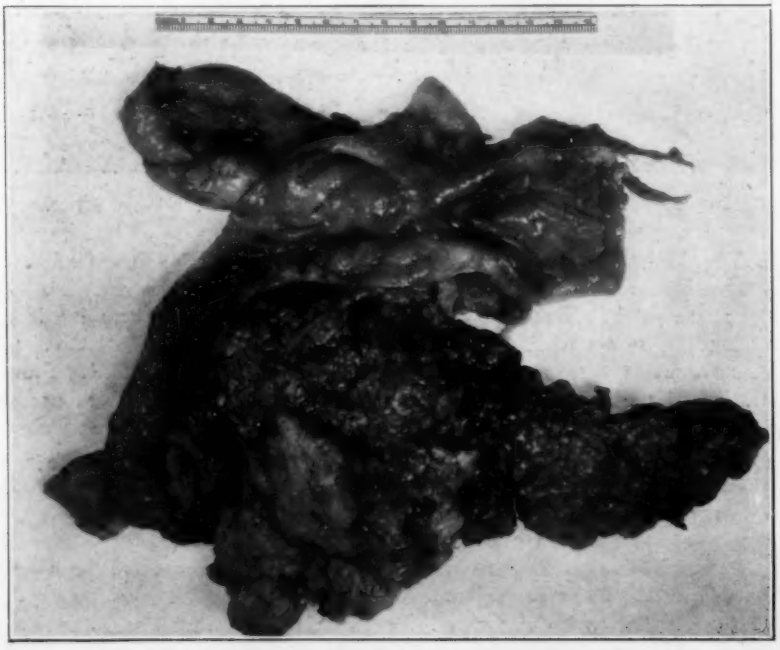

Fig. 3.—Pancreas with attached duodenum in case of acute pancreatitis—fat necrosis, associated with bilateral lobar atelectasis.

The left lung weighed 300 Gm., the right, 320 Gm. With the left lung in situ only a narrow margin of the lower lobe was visible. The upper lobe was of a pale bluish-gray cast with dull slate-colored mottling. The right lung in situ was similar to the left lung. The pulmonary artery was opened without disturbing the organs and was found to be normal. The trachea and the first division of the bronchi were opened and were found to be clean. The lower

Fig. 4.—Lobar atelectasis, showing obliteration of the alveolar spaces by apposition of the interalveolar walls; × 160. Note that blood vessels are free from thrombi.

lobe of the left lung was limp, flabby and airless, and its pleural covering was clean and glistening except for a small area about 3 by 1 cm. which was covered with a loose fibrous adhesion. The cut surface of the lower lobe was homogeneous in appearance. A small amount of blood-stained material was obtained only on

continued scraping. The cut surface of the upper lobe was pale pinkish-gray and was moist. The right lung was similar to the left except that there was an atelectatic area at the base of the middle lobe which was identical in appearance with the lower lobe (fig. 2).

The pancreas was soft dark reddish-gray; it was friable and of about the same appearance throughout. On account of shaggy-lined crypts filled with friable, dark gray material, the surface was uneven (fig. 3).

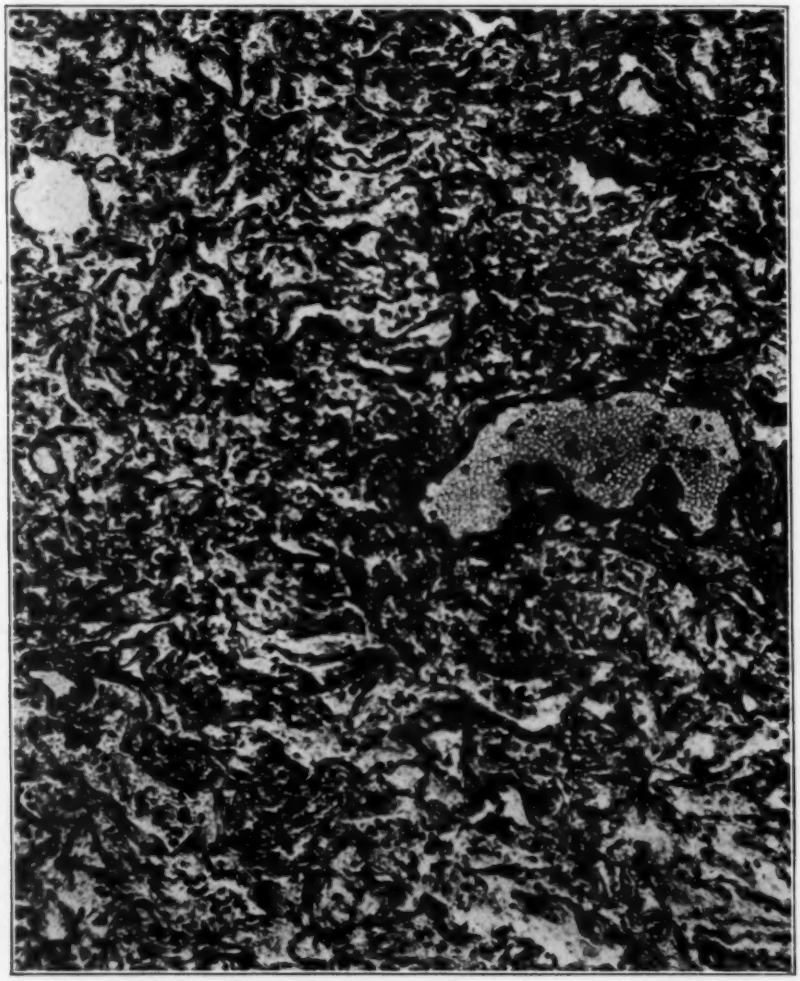

Fig. 5.—Lobar atelectasis, showing apposition of many of the interalveolar walls, and the presence of serum and red blood cells in the alveoli; × 160. Note absence of thrombi in both arteries and veins.

The falciform ligament was 4 cm. to the right of the midsternal line. The lower border of the right lobe of the liver was 10 cm. below the costal margin in the right midclavicular line. The edges were slightly rounded and the surface of the organ was smooth. The cut surface showed normal lobular markings.

The serosa of the gallbladder was smooth and clean. The organ was slightly ballooned and was filled with dark tenacious bile containing numerous small soft yellowish faceted stones averaging 3 mm. in diameter. On squeezing the gallbladder, bile flowed from the ampulla of Vater.

Microscopic Observations.—Sections through the atelectatic area showed the interalveolar wall to be in apposition. Some of the alveoli of the lungs contained mononuclear leukocytes, serum and red blood cells. The bronchi contained mononuclear leukocytes. With the exception of the lining cells of the alveoli, which were more cuboidal, the alveoli were normal in appearance (figs. 3 to 5).

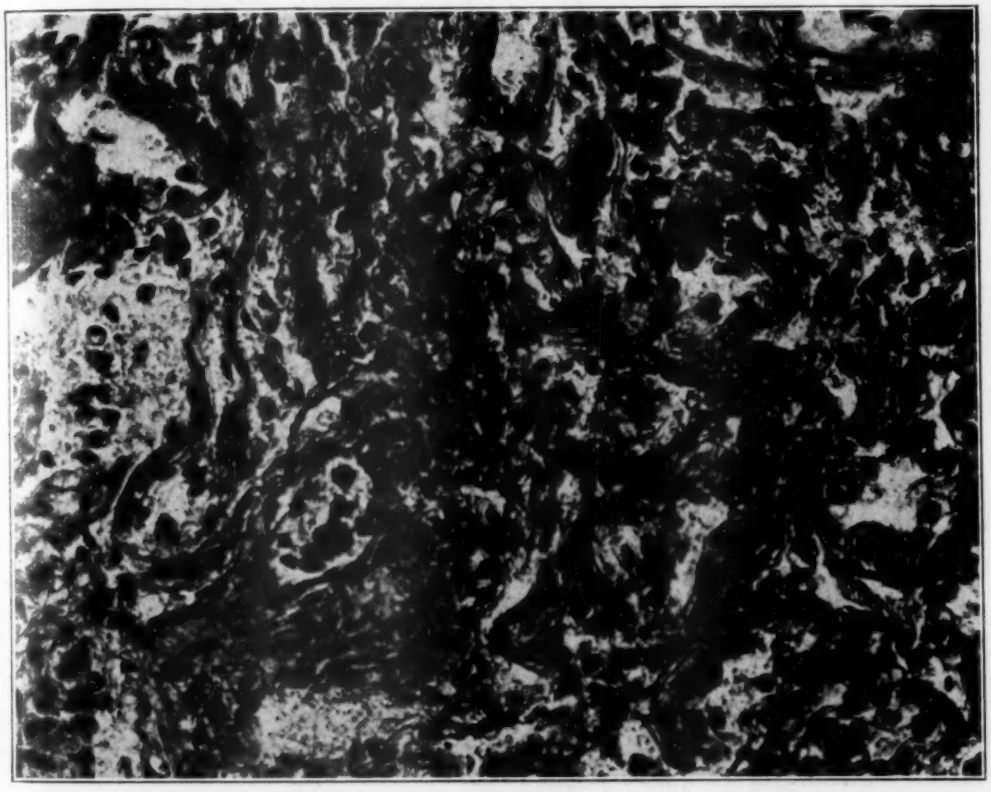

Fig. 6.—Lobar atelectasis, showing the lining cells of the alveoli have become cuboidal or rounded as the result of contraction of the alveoli; ×250.

There were intact scattered islands of parenchyma in the pancreas which stained normally. The remaining tissue when stained presented a neutrophilic indistinguishable mass without histologic markings (necrosis). No leukocytic reaction was apparent except for an occasional clump of polymorphonuclear leukocytes at the periphery of the necrotic area (figs. 6 to 8).

Anatomic Diagnosis (Gross and Microscopic): The following anatomic diagnosis was made: (1) Acute pancreatitis (fat necrosis); (2) lobar atelectasis, bilateral; (3) cholecystolithiasis; (4) hydroperitoneum (ascites); (5) obstruction of the foramen of Winslow, and (6) recent laparotomy wound.

COMMENT

The term atelectasis is used here to denote the condition of the lung in a collapsed state. Although the term atelectasis of the lung is usually used to designate the complete or incomplete failure of the lung of the new-born to expand, nevertheless, no other term describes collapse of the lung of unknown etiology as well, especially when the etiology of this condition appears to be a lack of expansion, as shown in the foregoing case.

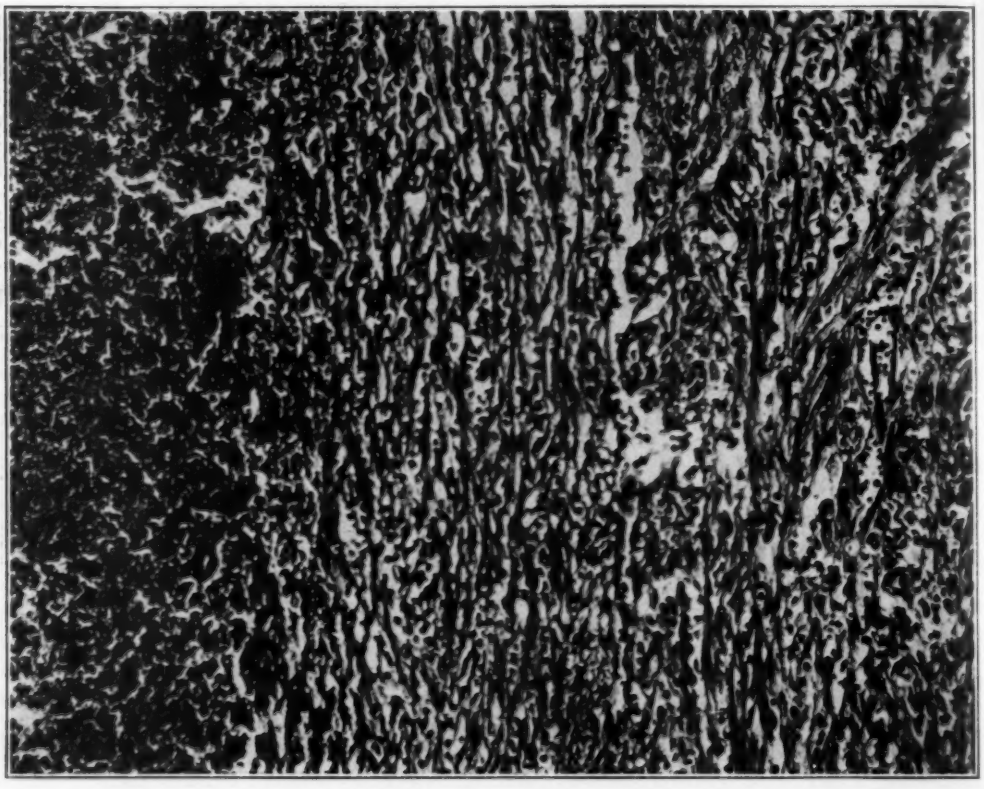

Fig. 7.—Acute pancreatitis—fat necrosis, showing absence of parenchyma and marked polymorphonuclear reaction; × 160.

This lesion has never been experimentally reproduced except by ligating the bronchi. The use of plugs in a bronchi never produces atelectasis unless the bronchi are completely occluded. The severing of both phrenic nerves does not produce the lesion, nor is it found in many cases of paralysis of the diaphragm. An evident factor in the production of atelectasis which has not been considered, but which evidently is present, is fixation of the diaphragm. This factor we believe to have

been present in the case here reported. Keith [1] has called attention to the different factors concerned in the expansion of the upper and lower lobes of the lungs. The lower lobe is independent on the excursion of the diaphragm and lower intercostal muscles. The upper lobes are expanded by the action of the upper intercostals, the scaleni and the accessory muscles of respiration. It should be noted that paralysis of the diaphragm resulting from a lesion of the cord or from severing of the phrenic nerves does not prevent the ascent and descent of this

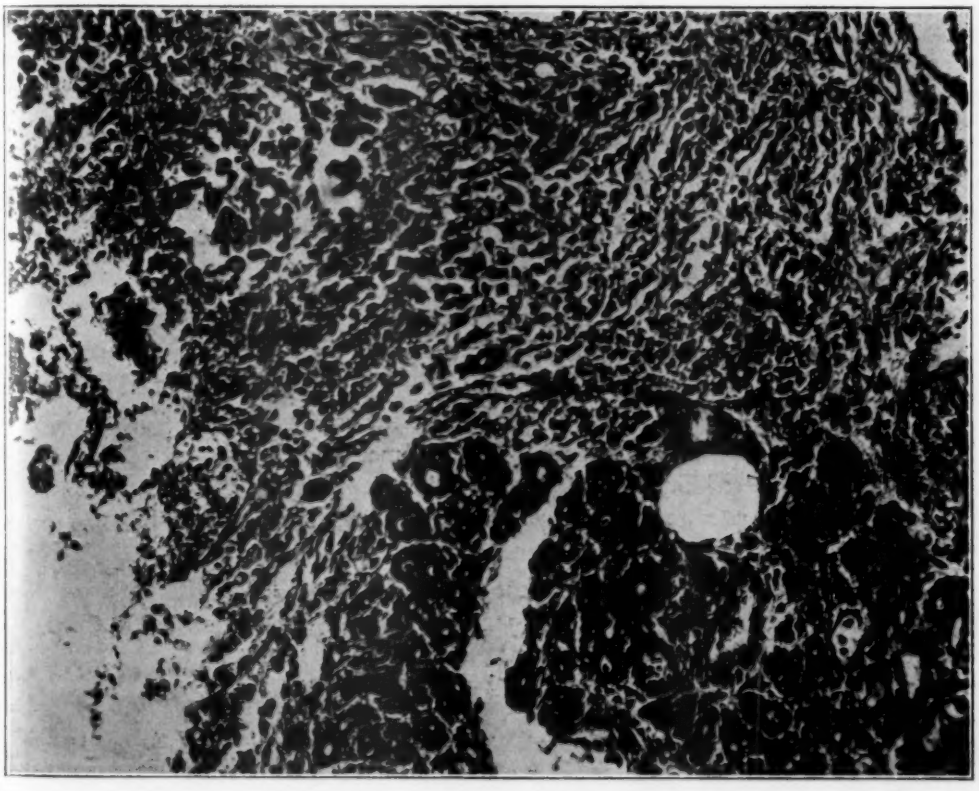

Fig. 8.—Acute pancreatitis—fat necrosis—, showing the presence of only a few parenchymatous cells; × 160.

structure since it is then in a flaccid state and subject to intrapleural and intra-abdominal pressures. As in this case, fixation of the diaphragm evidently was present, the lesser peritoneal cavity was distended with fluid. Though the onset of the illness was evidently due to acute pancreatitis, three days later the patient had a transient cyanosis which is

1. Keith, cited by Soltau, A.: Massive Pulmonary Collapse, Brit. M. J. **1**:544 (March 21) 1925.

typical of collapse of the lung. The roentgenogram taken five days after the acute onset of the illness shows what was probably a bilateral atelectasis of the lower lobes.

That the circulation continued through the atelectatic areas was well shown by the clean, glistening pleural surface and also by the well preserved structure of the interior of the lung. This of course would mean that a certain percentage of nonaerated blood returned to the left side of the heart. In the average patient, this deficient oxygenation of the blood would not be serious, but in cases of hyperthyroidism in which the oxygen consumption is greatly increased and also in cases of low cardiac reserve, this is a serious and sometimes a fatal complication.[2]

It is often stated in reports of cases of postoperative collapse of the lung that lobar pneumonia was a probable complication. In this case there was no pneumonic process and presumably the lungs in a patient of lowering resistance had been in a state of atelectasis for fourteen days. Impairment of the circulation in the aelectatic area was not sufficient to be evident.

SUMMARY

1. A case of bilateral lobar atelectasis in a woman, aged 48, is reported, the onset occurring three days after the onset of an acute pancreatitis (fat necrosis).

2. The observation that the lesser peritoneal cavity was distended with serum and the foramen of Winslow mechanically obstructed suggested the possibility that fixation of the diaphragm was the greatest factor in the production of a spontaneous collapse of the lower lobes of the lungs.

3. Collapse of either the upper or the lower lobe might be produced experimentally by removing all factors which are concerned in the production of the expansion of these lobes in the normal respiratory excursion.

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2. Ball, R. P.: Lobar Atelectasis Following Thyroidectomy and Lobectomy; Report of Four Cases with Necropsy Findings, to be published later in *Arch. Path.*

SURGERY OF THE LUNG

CARE OF THE STUMP IN PNEUMECTOMY AND IN LOBECTOMY *

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Surgical treatment of the thorax is not a new field. Written records of thoracotomy in empyema and the recognition and drainage of pulmonary abscesses can be traced as far back as the time of Hippocrates in the fourth century B. C.[1] Hippocrates gave a detailed description of the course of pneumonia with the development of empyema and the steps of thoracotomy for the drainage of empyema. He recognized the development of pulmonary suppuration and regarded aspiration as the cause of it. After the time of Hippocrates, the subject was neglected until the beginning of the sixteenth century A. D., when Schenk, in 1584,[2] drew attention to this field. From that time on there were occasional reports of thoracotomies, and a great impetus was noticed with the introduction of methods of inducing artificial respiration by the Sauerbruch, the Brauer or the Meltzer technic. From this time on, thoracic surgery began its inception as a distinct specialty. In his brief but inclusive article, Willy Meyer[3] classified various operations on the lung that had been devised up to that time under four headings:

1. A single mass ligature around the bronchus and its vessels; amputation; cauterization of the mucosa of the stumps with pure phenol or the Paquelin cautery.

2. A single elastic mass ligature around the hilum and the removal of the lung at a second procedure ten days later (Lenhartz).

3. Ligature and division of the main bronchus with the remnant of the lung tissue stitched over the stump (Garré).

4. Isolation and temporary clamping of the bronchus; curetting of the bronchus; tight silk ligature; a second loose catgut ligature placed more centrally around the bronchus (Friedrich).

Meyer described a method for pneumectomy that he had found successful. The steps of his procedure are as follows: (1) isolation of

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1. Hippocrates: E. Littré Edition, 1851. Περὶ νούσων τὸ δεύτερον, vol. 7, chapter 44, p. 62, and vol. 7, chapter 57, p. 88; Περὶ τῶν ἐντὸς παθῶν, vol. 7, chapter 3, p. 174.

2. Schenk, quoted by Murphy, J. B.: Surgery of the Lung, J. A. M. A. **31:** 151 (July 23) 1898.

3. Meyer, Willy: Pneumectomy with the Aid of Differential Air Pressure: An Experimental Study, J. A. M. A. **53:**1978 (Dec. 11) 1909.

the bronchus, (2) clamping and crushing of the bronchus, (3) ligation and amputation and (4) burying of the stump and the use of top sutures. By using this technic, Meyer encountered only four deaths in twenty-one dogs on which total excisions of the lung were performed.

Other modes of handling the stump were developed from time to time. Thus, Halsted [4] performed twenty-one consecutive operations, and in only one was there primary infection of the pleura. He first isolated the bronchus; after bisecting it and removing the mucosa, he sutured the flattened edges together and held them with a series of sutures around the edges together with interrupted through and through sutures which encircled the cartilages.

Quinby and Morse [5] obviated the difficulty of pushing a large crushed portion of the main bronchus by treating each of the primary bronchi separately with the use of the technic employed by Willy Meyer.

Giertz [6] used a transplant of fascia lata to cover the crushed bronchial stump which was first sutured with silk mattress sutures.

Lilienthal [7] devised an ingenious technic for lobectomy. He applied a chain of pedicle suture ligatures and then excised the lung, leaving a generous stump. The ligatures were left long and were included in a rubber dam pocket, which prevented any of the remaining intrathoracic viscera from coming in actual contact with the stump. The rubber dam and the ligatures slough out and leave a healthy stump when they are removed.

It will be noticed that in practically all of the procedures mentioned little if any attention is paid to the vascular supply of the lung or the control of hemorrhage. I agree with Friedrich [8] that in surgical treatment of the lung hemostasis is the least troublesome factor, and that the success or failure of the operation depends on making a completely air tight stump. A few other factors must always be taken into consideration in operations on the lung. First, the lung expands and contracts with each respiratory movement so that the contiguous lobes interfere and make it necessary that they be packed away with wet gauze so that injury will not be produced. At times even a slight puncture with the needle or the tip of the knife causes an unnecessary amount of trouble-

4. Halsted, W. S.: Clinical and Experimental Contribution to the Surgery of the Thorax, Tr. Am. Surg. A. **27**:119, 1909.

5. Quinby, W. C., and Morse, G. W.: Experimental Pneumectomy: The Application of Data so Obtained to the Surgery of the Human Thorax. Boston M. & S. J. **165**:121, 1911.

6. Giertz, K. H.: Ueber extirpation von Lungen und Lungenlappen mit Versorgung des Bronchial stump fes durch frei transplantierte Fascia lata, Zentralbl. f. Chir. **41**:1433, 1914.

7. Lilienthal, H.: Thoracic Surgery, Philadelphia, W. B. Saunders Company, 1926, vol. 2, pp. 147-169.

8. Freidrich, P. L.: Thoracic Surgery, J. A. M. A. **53**:1970 (Dec. 11) 1909.

some leakage of air and blood and makes it necessary to suture the lung by using either the Sauerbruch, Garré or a purse-string suture. Such an accident prolongs the operation and produces a greater tendency for shock and infection. Another important factor that aids in the success or failure of an operation on the lung is the length of time required. The quicker the operation is terminated, the better chance the subject has for recovery. By a mere thoracotomy the pressure relations of the intrathoracic and intra-abdominal organs are suddenly disturbed. In spite of the fact that intermittent positive pressure artificial respiration is maintained, and thus a stretching of the vessels of the lung provided for, as yet provision has not been made for the sudden increase of pressure exerted on the heart. Thus, the sudden and profound changes that occur in the circulation must be taken into account. I have often watched the heart become suddenly slow in rate and irregular in rhythm for no apparent reason, and only an injection of epinephrine or hydrochloride ephedrine would relieve this condition. In this case, if the heart is not stimulated promptly by means of an intracardiac injection of the drug, the animal either dies on the table or soon after the operation is performed. Another important factor that must always be considered is the sudden change in the temperature of the intrathoracic organs as a result of the thoracotomy. This sudden chilling undoubtedly has a definite injurious effect and must be prevented as much as possible. An important factor, indeed, is the manipulation and exposure of the virgin pleural cavity. The pleural surfaces are secretory and, like the peritoneal surfaces, any chemical, bacterial or mechanical irritation will produce an inflammatory change of a varying degree with subsequent exudation of serous fluid which has a tendency to change into a fibrinous and, later, a fibrous exudate, thus causing adhesions. The peritoneum has the same relation to the abdominal cavity as the pleura has to the thoracic cavity. It is inconceivable to think that a varying degree of pleuritis does not follow a thoracotomy. The most important consideration in surgical treatment of the lung is the upkeep of the process of oxidation in the body. I have found that dogs with an open pneumothorax do not live longer than ten minutes, at the most, after an intercostal opening of from 10 to 12 cm. Meltzer's insufflation anesthesia, which provides for a constant stream of air, is not satisfactory because it distends the lungs but does not make provision for contraction of the lungs. It is necessary that there be an intermittent blast of air so that an intermittent stretching and relaxing of the vessels of the lung may take place and thus the pulmonary circulation be kept up. In a series of experiments by means of which a sufficient amount of oxygen was supplied, a bilateral artery to vein transfusion being used, which was termed cross circulation, it was possible to double the length of life in the presence of an artificial pneumothorax. In these cases the lung stayed collapsed,

so that after the blood left the systemic circulation and entered the pulmonary circulation it encountered considerable resistance. As a result, a gradual engorgement in the lung of the recipient and a depletion of blood in the animal used as a donor were noticed. Thus, the donor died of an acute hemorrhage and the recipient of asphyxia and cardiac collapse. An intermittent artificial respiration obviates all this difficulty, because it not only supplies the lung with oxygenated air and provides for elimination of the carbon dioxide that is formed as a result of respiration, but it provides for the intermittent stretching and relaxing of the capillaries of the lungs that are so important in the welfare of the circulation of the blood.

Another factor of some importance is the disturbance to the vagus trunk of its branches as they enter the lung. In lobectomy, such as the Meyer type, one necessarily has to disturb the vagus. Under such conditions the heart, the circulation and the gastro-intestinal apparatus may be disturbed by the abnormal stimulation of the vagus. A factor recently was brought to my attention in some experimental lobectomies. In prolonged handling of the lung, an acute dilatation of the stomach, which proved fatal to the dog, was noticed. The difficulty was traced to a disturbance in the pillars of the diaphragm.[9] This disturbance may result indirectly through the lungs or directly through injury to the phrenic nerve or disturbance of the diaphragm itself.

With these facts in mind it becomes evident that one must find a method which will be simple and can be completed rapidly. It should control both the aeration and the vascular supply of the lung. It should provide for the avoidance of any unnecessary chilling or drying of the intrathoracic organs. I feel that the technic that is proposed here will satisfy the majority of these factors.

PROCEDURE

After a preliminary shaving of the dog and cleansing of the skin with soap and water, the skin is sterilized with tincture of iodine. The animal is now covered with sterile sheeting, and only the field of operation is left exposed. An incision is now made in the skin parallel to the ribs, and the platysma and latissimus dorsi are exposed. These muscles are incised in the direction of their fibers and are spread open so that the least amount of injury is caused to the muscles. These muscles are later utilized to cover the intercostal incision tightly. The intercostal space now comes into view. At this point I make sure that the epinephrine or ephedrine solution is ready for instant use. I also have the anesthetist get the apparatus for administering artificial respiration ready. The artificial respiration is now started, and a small nick is made down into the chest. As soon as the pleura is pierced, one can hear a wheezing. The incision is now enlarged by means of the finger or a blunt instrument. At this point artificial

9. Hedblom, C. A., and Joannides, M.: The Relation of the Hiatus Esophageus to the Stomach. An Important Function of the Pillars of the Diaphragm, to be published.

respiration is stopped, so that the lung collapses, and in this way it is not torn when the intercostal incision is enlarged. This incision is usually made with the scissors. As soon as it is felt that a sufficiently large opening has been made in the chest, the artificial respiration is resumed and just enough pressure is exerted so that the lung expands and fills up the whole cavity of the chest.

The ribs are now spread apart with a self-retaining retractor, and the lung is pulled out by means of tissue forceps without teeth. At this point the artificial respiration is stopped again so as to allow the lung to collapse. Then a Kocher or Moynihan intestinal clamp with rubber tips is applied to the hilum (fig. 1). Just enough pressure is exerted with the clamp to stop the hemorrhage and control leakage of air when the lung is cut. Only a slight pressure is required for this clamping because the pressure in the lesser circulation is low, and the positive pressure in the artificial respiration apparatus is also low. Care must also be taken not to crush the tissues so that they will not slough. Artificial respiration is now started again and continued until the chest is closed.

Gauze moistened in hot saline solution is now used to protect the unexposed tissues and at the same time to catch any blood that will run out when the lung is cut. An attempt should be made to take out a wedge, and enough lung tissue must be left to cover over the stump (fig. 1). The lung should be cut at least 1 cm. distal to the compressing clamp. The bronchi are now isolated and ligated. The large vessels are also ligated. The suture is now started at the middle of the incision. This first suture is tied, but the end is left long so that it can be used later. A bite is now taken first on one and then on the other side of the first suture in such a way that the two sides of the wedge are brought in apposition. When the raw surfaces have all been covered with pleura, the compressing clamp is released and at the same time the suture is gently tightened. This maneuver accomplishes a double purpose. It allows the cut portions of the lung to become approximated more tightly, and at the same time it gives one an opportunity to look for leakage of air or blood. If the stump is airtight and watertight, the compressing clamp is removed and the chest is closed. If, on the other hand, the stump is leaky, the compressing clamp is retightened and additional interrupted sutures are used to cover the defect. The clamp is now removed, and the stump is left to drop back in the chest. Any blood that has found its way in the chest is now removed, and the chest is closed. In some experiments, the phrenic nerve is cut just before the chest is closed in order to produce a paralysis of the diaphragm and thus reduce that chance for suction through the stump. If the phrenic nerve is cut, care must be taken to ligate the pericardiophrenic artery, which is intimately attached to the nerve. In one case death was caused by hemorrhage from this vessel. Three fine wires are now used to aid in the approximation of the ribs. As they are inserted in the intercostal spaces with a number 1 or number 2 cutting needle, the underlying tissues are protected by means of a spatula which is placed on the parietal surface of the wall of the chest. In addition to the wire sutures, three interrupted heavy silk sutures are placed with the wires. The wires are pulled together, and thus the ribs are approximated. The silk sutures are tied and as soon as it is noticed that wheezing does not occur with each respiration, the artificial respiration is stopped. The overlapping muscles are now approximated and the wound is closed without drainage.

Care must be taken not to handle the heart or the pericardium any more than is necessary, because even the slightest handling has caused definite cardiac irregularity in the rhythm. The heart must be watched at all times and as soon as any slowing in the rate associated with cyanotic blood is noticed more air must

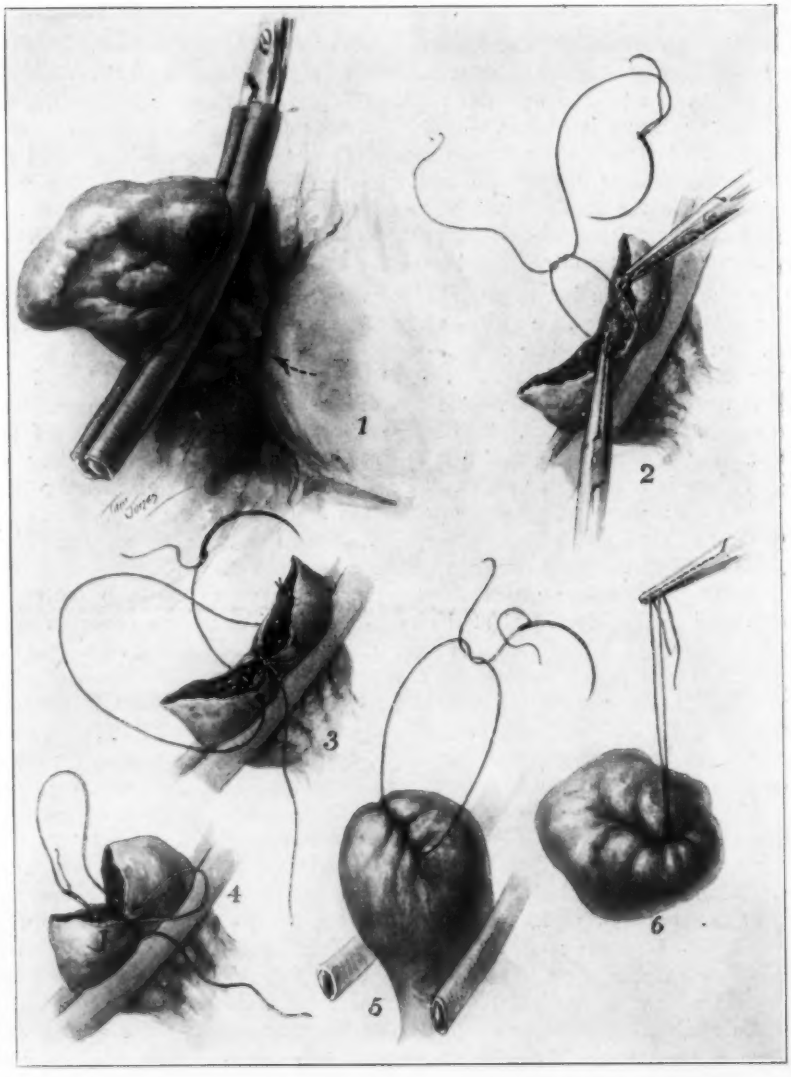

Fig. 1.—The important steps in the care of the stump. In *1*, the arrow indicates the constricting clamp applied to the root of the lung; *5* shows the constricting clamp released and the suture tightened and *6*, the appearance of the stump after the final knot is tied.

be given and also an intracardiac injection of 1 : 1,000 solution of epinephrine hydrochloride or 1 per cent solution of ephedrine must be administered. One cubic centimeter has been used with good results.

For artificial respiration, compressed air, which is forced into the lungs through a tin mask, has been used. The tubing is so arranged that either air alone or air saturated with ether can be given. If a varying degree and length of pressure on the floor of the mouth is applied in the dog, the amount and also the pressure of the air that is introduced into the lung can be regulated. The length and the degree of compression must be such that the lung distends to its full capacity in the open chest.

RESULTS

Fifty-four partial or complete pneumectomies were performed on dogs. Nine of these animals died on the table during the earlier period of the experiments. As my associates and I became more expert in technic and as accidents and emergencies were watched for, the point was reached where the dogs survived the effects of the operation and lived for a long time. Of the nine that died on the table, six died of asphyxia caused by unsatisfactory artificial respiration. One dog died as a result of an accidental acute hemorrhage from the pulmonary artery. This hemorrhage resulted from the premature release of the compressing clamp at the hilum. The clamp could not be easily reapplied, and by the time it was reinserted the dog was exsanguinated. Digital pressure was not thought of until it was too late. Two other dogs died as a result of an acute dilatation of the stomach. This dilatation was encountered frequently, but two dogs were killed before it was found that a prompt emptying of the stomach with a tube was all that was needed. Another factor that shortened the postoperative life of the animals was distemper. Nine dogs developed this disease, and all died as a result.

All of the dogs showed evidences of pleural irritation with a greater or lesser amount of exudation. In those that died during the first ten days the chest was found full of serosanguineous exudate which would not clot either in or outside of the chest. Such a fluid was present on both sides. I believe that the fluid found its way into the opposite side through the thin mediastinum of the dog. Such has been my experience when fresh blood was injected into one side of the thorax. When the animal was killed two days later, the blood was present in about equal amounts on both sides. The site of suture was always found to be adherent to the wall of the chest and generally at the site of the thoracotomy. In the first ten days, the adhesions were fibrinous or a weak fibrous type. As the interval became longer the adhesions became stronger, so that in some cases the stump could be separated from the wall only by means of a sharp dissection (fig. 2).

Infection and leakage were encountered in one stump. In this experiment, an undue amount of strength was used to tie the suture and thus necrosis and a slough were caused.

During the first week the stump was dark purple and presented little crepitation. During this period, areas of hemorrhage into the interstitial tissue and the alveolar spaces were seen microscopically. At the site of the suture, the alveolar spaces were compressed in one direction and thus were changed into strands of tissue (figs. 3 and 4). The bronchioles

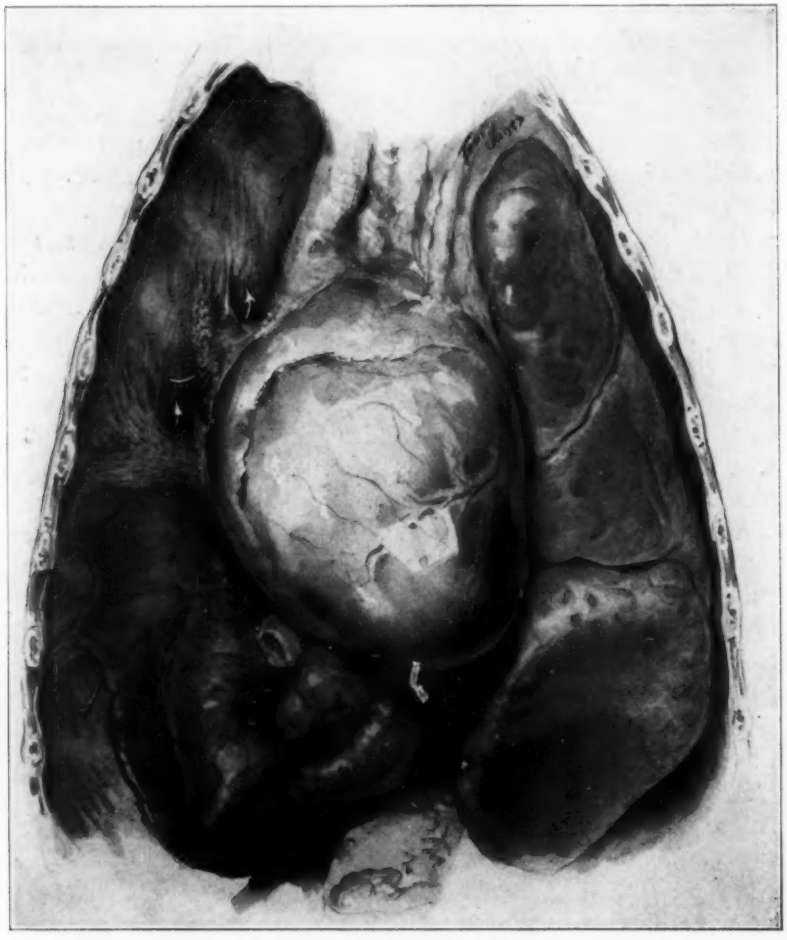

Fig. 2.—Appearance of the stump thirty-two days after an upper right lobectomy with the author's technic. The scar tissue binding the stump to the wall of the chest and pulling the mediastinum to the right side should be noted. The arrow points out the communications above and below the stump. Pathologic change did not occur in the lung or pleura on the left side.

were also compressed, and in the larger ones plication of the mucosa was encountered. In some areas beginning production of granulation tissue with loss of alveolation was seen.

In the later stages it was found that the stump again assumed its normal color and had areas which showed crepitation, but the site that was exposed was found firmly adherent to the nearest portion of the wall of the chest. The strands of compression near the suture and also flattening of the bronchioles were seen microscopically. Some bronchioles lost their major characteristics and could be recognized only by the cartilage or the remnants of bronchial epithelium. In some areas an entire loss of alveolation was found, and the whole field contained dense fibrous tissue. In the crepitating areas, the characteristic alveolation but also a characteristic increase in the interstitial fibrous tissue

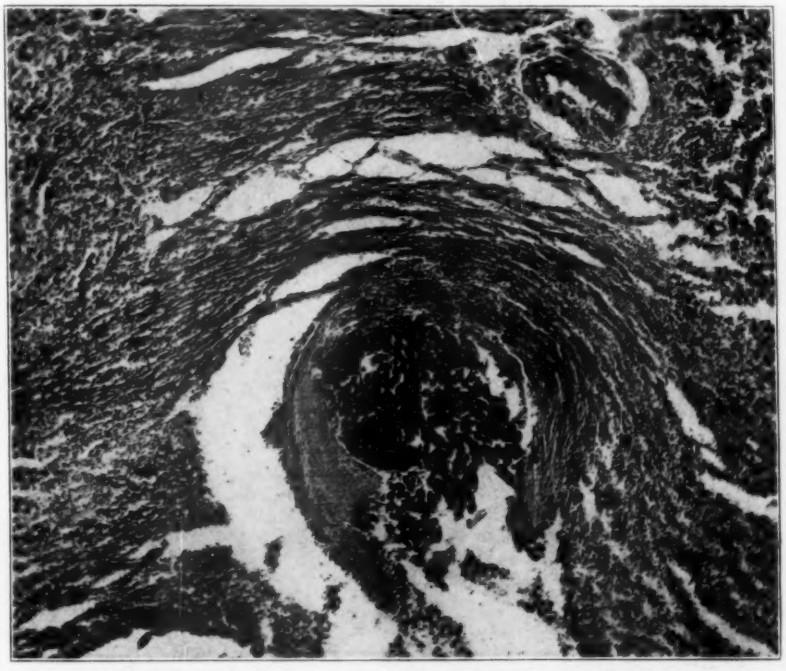

Fig. 3.—Section from the stump eighty-one days after lobectomy. The strand formation of the alveoli caused by the silk suture should be noted.

with proportional decrease in the size of the alveolar spaces have been found.

In the presence of infection, changes characteristic of pneumonia were noticed as well as areas in which there was a localized deposition of polymorphonuclears but no destruction of the center. In such cases, lobar pneumonia in the contiguous lobe and even on the opposite side was also noticed.

In all cases, a thickening of the pleura around the stump was found. This thickened pleura and the adhesions are the best allies in giving good results.

The contiguous lobe or the lung on the opposite side may show any of several changes. It may remain normal; it may show lobar pneumonia, edema, and, most frequently, an interstitial thickening.

Secondary operations on the same or opposite side have not been borne well by these dogs. It is possible that the anesthetic has something to do with it. Ether has been used throughout. One animal, which was thought to have recovered completely, was operated on 101 days after the first operation. This dog died on the table in the middle of the operation. It did not take the anesthetic well in spite of the satisfactory anesthesia and artificial respiration.

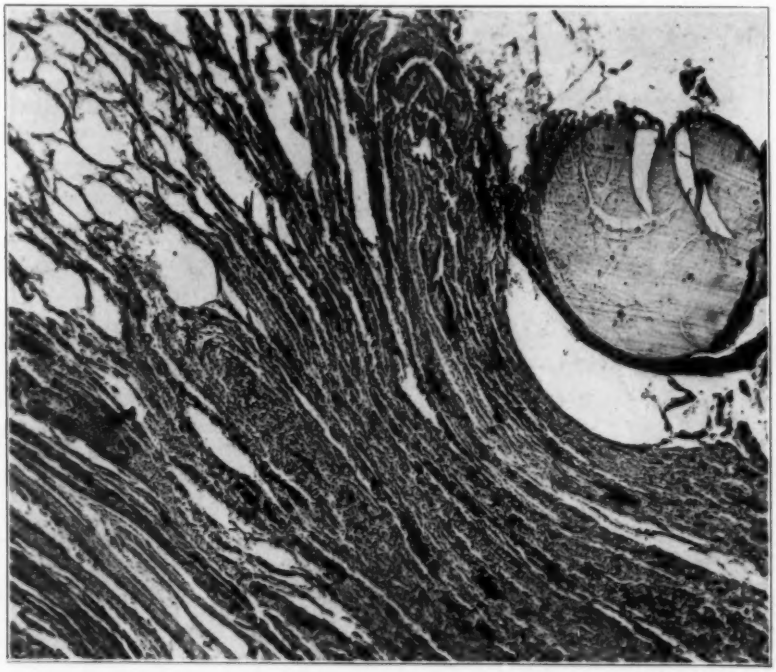

Fig. 4.—Section from the stump 101 days after lobectomy. The strand formation of the alveoli at the point of compression and the gradual return to normal alveolation beyond the catgut suture should be noted.

COMMENT

The results in these experiments were encouraging. In only one case were infection and leakage of air at the stump encountered. In all the others, the stump remained airtight and watertight. It was noticed that when the dogs were left alone after the operation they might live indefinitely, if they survived the first six days. It is possible that the removal of a lobe or the whole lung will cause a definite strain on the circulation, with a subsequent acute or subacute edema which eventually causes asphyxia in the dog. Moreover, if the wall of the chest is left

rigid, a dead space is left on the side on which the operation was performed and thus exudation is induced, which may invite infection. In the experiments it was noticed that the less lung tissue removed the greater the chance for complete recovery. The method of leaving a certain amount of lung tissue to be used as a reinforcement over the bronchus is of distinct advantage. The danger of rupture in this stump is obviated first by the ligation of the larger bronchioles and also by the pneumothorax on the side on which the operation was performed. Another precaution is the production of temporary or permanent paralysis of the phrenic nerve at the end of the operation. This lessens the chance for an inspiratory suction action within the stump. If a stump of lung tissue is left, the pleural surfaces are approximated and thus a thick pleural covering is induced at the site of the resection of the lung. The fibrosis that occurs in the lung tissue of the stump adds to the efficiency of the operation.

In the operations in which the whole lung is removed and the bronchus is left exposed, none of the foregoing factors can be mobilized as aids. Moreover, the circulation, the vagus and the heart are disturbed by the unnecessary additional handling of the bronchus and its contiguous structures. Often it was found difficult to try such methods in ligating and suturing the bronchus without going through all its walls. Even with a perfect technic, the operation is much more prolonged than in the procedure employed in the present experiments. With the use of the technic described, it has been possible to complete the operation in from eight to twelve minutes from the time of the incision in the skin till the complete closure of the wounds. Our results with this type of operation are not different from those of Bettman.[10] The wall of the bronchus was found resistant, and the greatest difficulty has been in attempting to invert the stump.

CONCLUSIONS

The method described has been found satisfactory in experiments on the dog. It provides for a stump which eventually becomes strong and prevents any possibility of perforation of the bronchus. The method is simple, does not require any special instruments and can be finished in the shortest possible time. It provides for approximation of endothelial surfaces in a manner similar to operations on the gastro-intestinal tract or the blood vessels.

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10. Betmann, R. B.: Experimental closure of Large Bronchi: A Study of the Factors Concerned in Failure of Bronchi to Heal, Arch. Surg. **8**:418 (Jan.) 1924.

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ACUTE EMPYEMA

TREATMENT BY CONTINUOUS TIDAL IRRIGATION AND DRAINAGE DEPENDENT ON NORMAL RESPIRATORY MOVEMENTS *

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The closed method of drainage and irrigation of an empyema cavity offers many advantages, chief of which are: 1. The method is simple and easy of operation, the insertion of a tube through a trocar under local anesthesia requiring only a few minutes. 2. The pressure within the cavity can be released at any desired rate. 3. There is little care in the form of dressings. 4. The cavity is not continually sucking air. 5. So long as the junction of the tube with the wall of the chest is air tight, suction can be applied, thus reducing the pressure within the empyema cavity below the surrounding atmospheric pressure and thereby decreasing the size of the cavity by expanding the lung.

On the other hand, many arguments have been advanced against this method of treatment. The most important has been that the drainage is inadequate; the pus, which becomes thick, and fibrin collecting in the tube cause a damming up of the infected fluid within the chest. This results in an elevation of temperature, and necessitates the removal and reinsertion of the tube or considerable effort to dislodge the plug which causes the obstruction. Each blockage with a damming up of the pus delays convalescence, not only by the systemic effect of the absorption of toxins and bacteria, with the danger of septicemia and metastatic infection, but by the rapidly progressing positive pressure within the empyema cavity which delays the expansion of the lung, and at times goes so far as to increase the size of the cavity by pulmonary compression.

This positive pressure within the chest also causes the pus to dissect along the tube, which, in the absence of a bronchial fistula, is the only avenue of escape from the infected pleural cavity. The most favorable course is for the pus to reach the surface, soil the dressings and dissect from the wall of the chest the adhesive straps holding the tube in place. With the infection and sloughing of the tissues about the tube, it soon becomes so loose that the cavity can no longer be kept air tight; then one has none of the advantages of closed drainage, while the small opening is inadequate for open drainage. Only the unusual patient has gone for ten days to two weeks without having the tube changed or become loose, permitting air to leak in through the hole in the wall of the chest.

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The more unfavorable complication has been for the pus to reach the subcutaneous tissues and to dissect beneath the skin, at times causing an infection more serious than the empyema, and necessitating multiple incisions; occasionally, if not recognized early, it has led to a fatal termination. This danger is greatest when the hemolytic streptococcus is the organism that causes the empyema.

In the class of minor disadvantages may be placed the presence of thick pus, which makes the irrigation of the cavity slow and difficult; the tendency, as healing progresses, to overdistend the cavity which is tending to collapse; the leakage of pus around the tube, demanding frequent dressings; and the plugging of the tube, causing almost continuous irritation and annoyance to every one concerned in the care of the patient.

In considering various methods to overcome these difficulties, it was thought that the natural movements of the chest with their pumping action could be utilized to give a continuous irrigation, and at the same time avoid the possibility of forcing in fluid under pressure. The original plan was to use an inflow and an outflow tube, each equipped with valves. It was found, however, that a simple tidal flow through as short a tube as possible was entirely satisfactory and gave the least possibility of becoming obstructed. With a continuous flow in one direction, fibrin blocks the opening to the outlet tube, but with the tidal flow it becomes dislodged at the next inspiration when the fluid flows into the chest.

The irrigation apparatus shown in figure 1 was soon adopted. This consists of a rubber tube which is passed into the dependent part of the empyema cavity through a trocar thoracotomy wound, and just outside the chest is connected by means of a T tube with a rubber bag on one side and on the other with a rubber tube leading through a Y tube to an irrigation bottle above and a drainage bottle below. The rubber bag is strapped to the abdomen just below the trocar thoracotomy wound, placing it slightly below the level of the empyema cavity with the patient in Fowler's position. This gives a slight amount of suction at all times. Since the entire system is closed, it is impossible for air to enter if fluid is kept in the irrigation flask and the drainage tube is always, when unclamped, below the level of the solution in the drainage bottle. This statement presupposes that the empyema is not complicated by a bronchial fistula, and that the tube fits snugly within the opening through the wall of the chest. The bag can be entirely emptied and suction applied to the empyema cavity by removal of the clamp to the drainage bottle. When this condition has been maintained for the desired length of time and the bag is partially refilled, there is no possibility of causing a positive pressure within the empyema cavity. The bag is never completely distended and usually is only from one-fourth to one-half full.

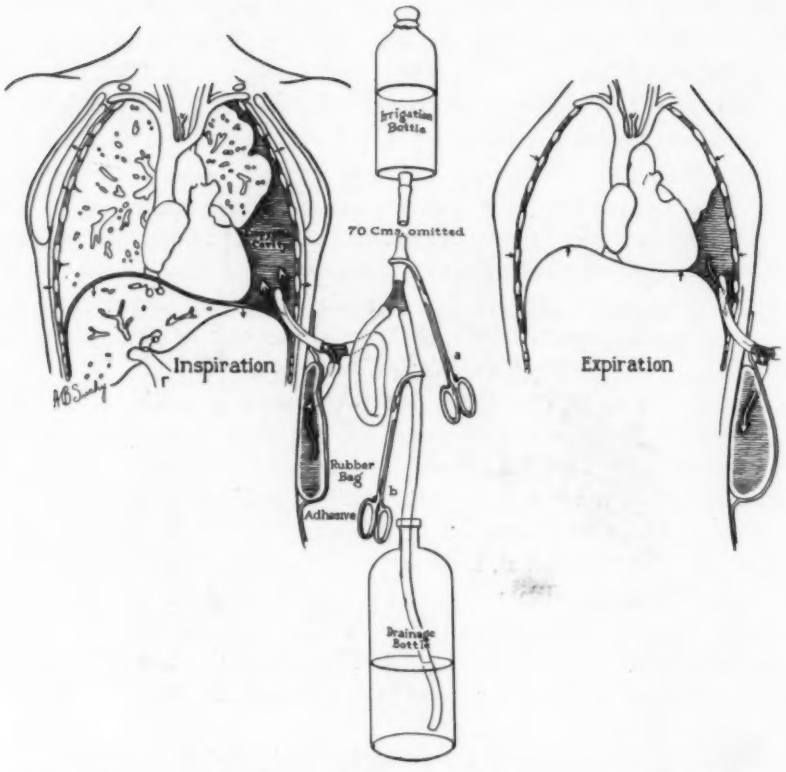

Fig. 1.—Diagrammatic illustration of the apparatus connected with the empyema cavity as shown in a cross-section of the chest. On the left is illustrated the effect of inspiration with enlargement of the thoracic cavity, and the reduction of the intrathoracic pressure below the surrounding atmospheric pressure. Thus the atmospheric pressure forces the fluid within the rubber bag strapped to the abdomen into the empyema cavity. With expiration, illustrated on the right, the intrathoracic space is passively or forcibly compressed with the outflow of air from the lungs and also of fluid from the empyema cavity, resulting in a diminution in the size of the cavity. This continues with each respiration, the consistency of the fluid within the empyema cavity and the rubber bag gradually approaching a common level. Before this is reached, however, clamp *b* is removed, the rubber bag is completely emptied, as much fluid as possible is siphoned from the empyema cavity, clamp *b* is reapplied, and clamp *a* is removed until the desired quantity of clean solution has flowed into the rubber bag and empyema cavity. The gradual mixing by means of the tidal flow again begins, and thus the consistency of the fluid within the empyema cavity gradually approaches that of the irrigating solution, the final point of dilution being determined by the amount of irrigation fluid kept in the bag, the frequency of its replacement, and the division of the time between irrigation and suction.

The frequency with which the fluid should be renewed within the bag depends on the individual case. Early in the treatment, or when the cavity is large, it is renewed every hour in order to keep the pus relatively thin, while later, when the cavity is small and clean, the bag can be refilled only a few times within the twenty-four hours. This avoids disturbing the patient at night, but at the same time gives him the advantage of continuous irrigation.

Fig. 2.—Irrigation apparatus in use. This photograph was taken after six weeks of treatment, the patient having a massive hemothorax with infection (figs. 3, 4, and 5). Not once during this time did the tube become plugged; the adhesive holding the tube in place was not changed during the first month, and the apparatus was out of order on only one occasion when the patient, while delirious, left his bed and pulled the irrigation bottle from its stand.

The proportion of time given over to suction and to irrigation depends entirely on the amount and rate of formation of pus. My plan has been to run the irrigation as much of the time as is necessary to keep the cavity clean and the contained fluid thin and relatively clear. The remainder of the time is given over to suction by the siphon. With the bag strapped to the body a little below the level of the empyema

cavity, and with the patient in Fowler's position, there is always a slight amount of suction, but not enough to prevent a free tidal flow.

For the most efficient interchange of fluid by the tidal flow, the amount of tubing between the empyema cavity and the rubber bag is cut to the minimum.

Numerous types of rubber bags have been tried, such as the Vorhees bag, blood pressure cuff, mouth piece for a gas anesthesia machine, and others. It is desirable, however, to have a bag with the tube entering it about the middle of the longitudinal axis; a football bladder best meets this requirement. There are two distinct advantages in this type of bag:

Fig. 3.—Close view of the apparatus shown in figure 2, and with the short tube strapped in the chest with adhesive; the tube to the football bladder, which had just replaced an old blood pressure cuff, was later shortened. The lower end of the bladder is turned in to diminish its size. The only care which this case demanded was observation for the proper distribution of the time between irrigation and suction, and renewal of the adhesive dressings about once every two weeks.

The first advantage is that all particles of fibrin and coagulated pus will settle to the dependent point away from the opening of the tube, so that when they enter the bag they are trapped. Incidentally, the tube in the chest entering at the dependent part of the empyema cavity tends to remove the thicker material as it settles out. The second advantage comes into play late in the treatment, after the tube in the chest becomes a little loose. At that time any air which may enter the irrigation system rises to the top and is trapped as soon as it is forced into the bag. The

thick pus and the air are removed when the fluid within the bag is replenished with fresh solution. Any bubbles of air in the tube to the irrigation bottle are likewise forced into the bag and trapped in its upper part when it is refilled with fresh irrigating fluid.

In the application of this apparatus, the fluid cannot be forced into the chest as long as the rubber bag is not more than from two-thirds to three-fourths full, and frequently it is kept only from one-third to one-fourth full. For children, the lower end of the bag is sometimes

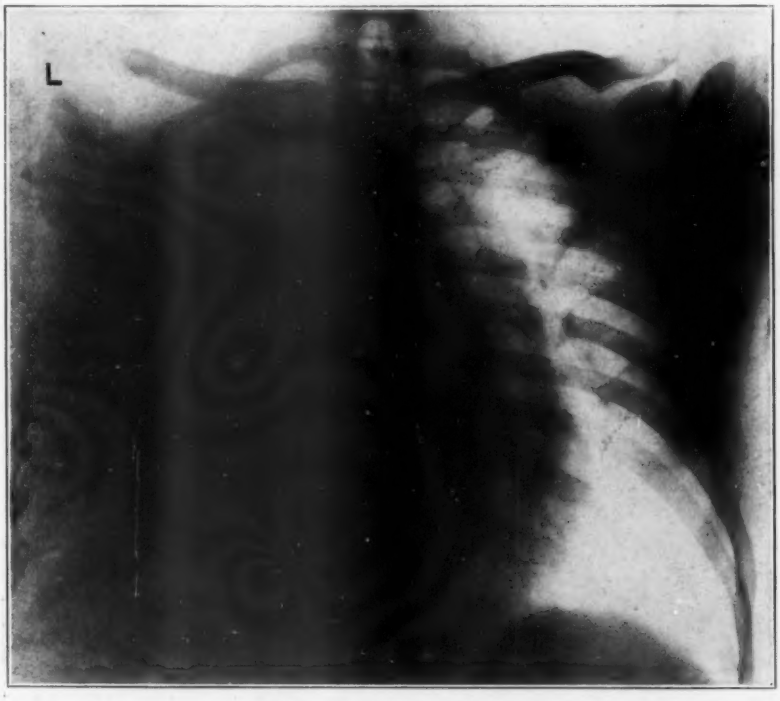

Fig. 4.—An enormous, infected left hemothorax following a stab wound of the chest. Over a period of two months repeated efforts were made to aspirate the fluid, but without result. The collection of fluid increased in size and there was a progressive rise of temperature until the clot became sufficiently fluid to aspirate. The fluid promptly reformed, the cultures were positive for *Streptococcus viridans*, and a trocar thoracotomy was performed.

turned in, as in figures 2 and 3, the size thus being decreased. This absence of positive pressure prevents the forcing of infected material out around the tube, particularly when the cavity has closed down until it holds only a few cubic centimeters, less than the amount of the tidal flow in the beginning of the treatment, and when one's tendency is to run in more solution than the cavity will hold.

The continuous movement of the fluid prevents any coagulation of fibrin and blocking of the tube. This has been proved by several patients

who have gone for from four to seven weeks without having the original tube removed or plugged at any time. One patient (figs. 2 and 3) went for a month without having the adhesive and small dressing about the tube removed, and at no time was there plugging of the tube or any cessation in the tidal flow of the fluid. Consequently, there was at no time any positive pressure of sufficient degree to force fluid out around the tube; also there was no suction of air as the tube fitted

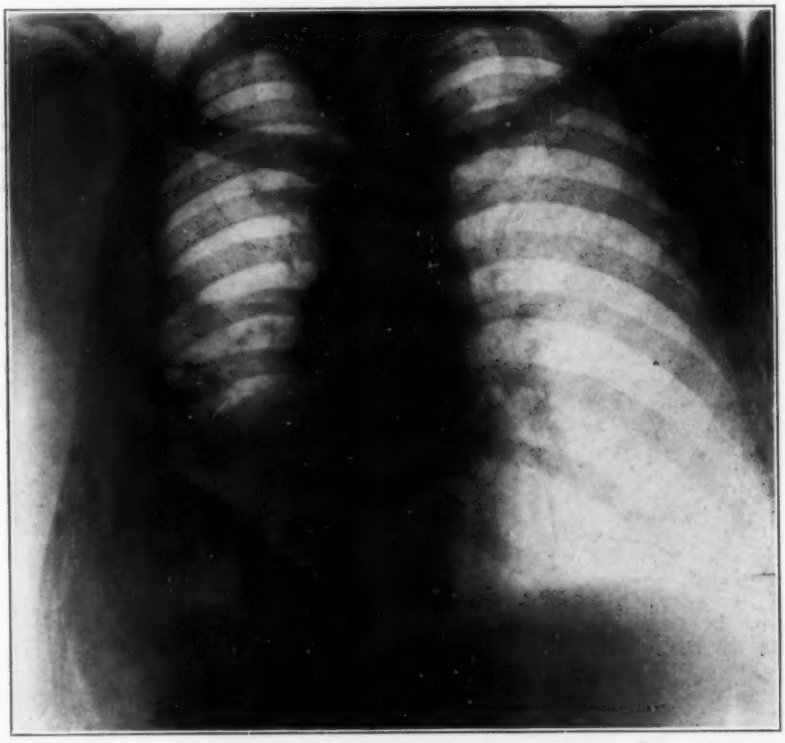

Fig. 5.—Same patient as figure 4, after ten weeks of treatment with continuous irrigation of, or suction on, the empyema cavity. The cavity had completely closed, and the temperature, which had been from 101 to 104 F. before operation, was below 100 F. after the fourth postoperative day. Note the high position of the diaphragm on the left side, its sharp rise from the midline outward until it fuses with the strip of thickened pleura. Below this point it is apparently adherent to the wall of the chest, thus helping to obliterate the empyema cavity after the long collapse of the lung.

The treatment in subsequent cases leads us to believe that the postoperative course here could have been shortened by giving more time to suction, by the earlier institution of forced expiration against an obstacle, with the lungs filled with air, and by inserting the tube through the chest at a lower level.

snugly. At the end of this time, the granulating sinus was free from excessive infection. Another patient went for eight weeks without

having the original tube removed and practically without leakage, the dressing about the tube being changed on several occasions.

In all cases, the cavity has been kept clean, the drainage fluid at no time, even with suction, being too thick to allow the ready transmission of light through the glass connecting tubes.

Suction can be applied to the cavity at any time, the nature of the residual fluid in the cavity determined, and the cavity irrigated by allow-

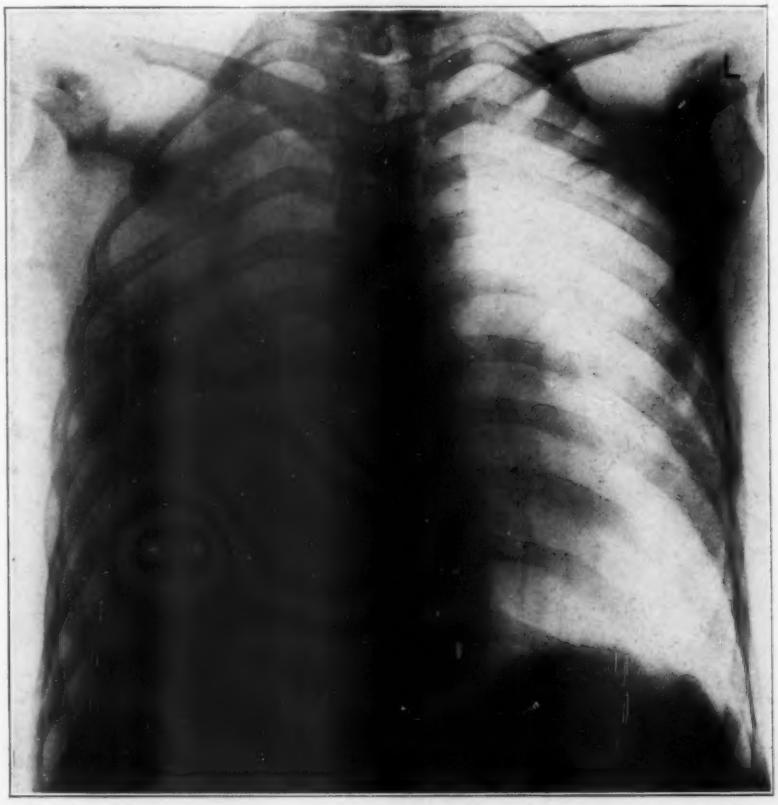

Fig. 6.—Condition of the chest on the day of operation in a case of acute streptococcus empyema following pneumonia. There had been repeated aspirations over a week's time.

ing clear fluid to flow in when the suction is released. Any percentage of the total time can be given over to irrigation or suction, depending on the turbidity of the fluid and the difficulty in keeping the cavity clean.

As soon as the more acute inflammatory condition has subsided, the patient can expand the lung and diminish the size of the cavity by blowing against some obstacle, as forcing fluid from a lower to a higher level. This, together with coughing, incidentally gives the maximum

tidal irrigation of the empyema cavity where the apparatus is in use. The blowing is also most efficient when this apparatus is applied, for there is absolutely free egress of fluid when pressure is made on the cavity by the forced expiration. Suction can be applied as desired to hold the lung in the position of expansion or to aid in the expansion obtained by forced expiration with the lungs full of air.

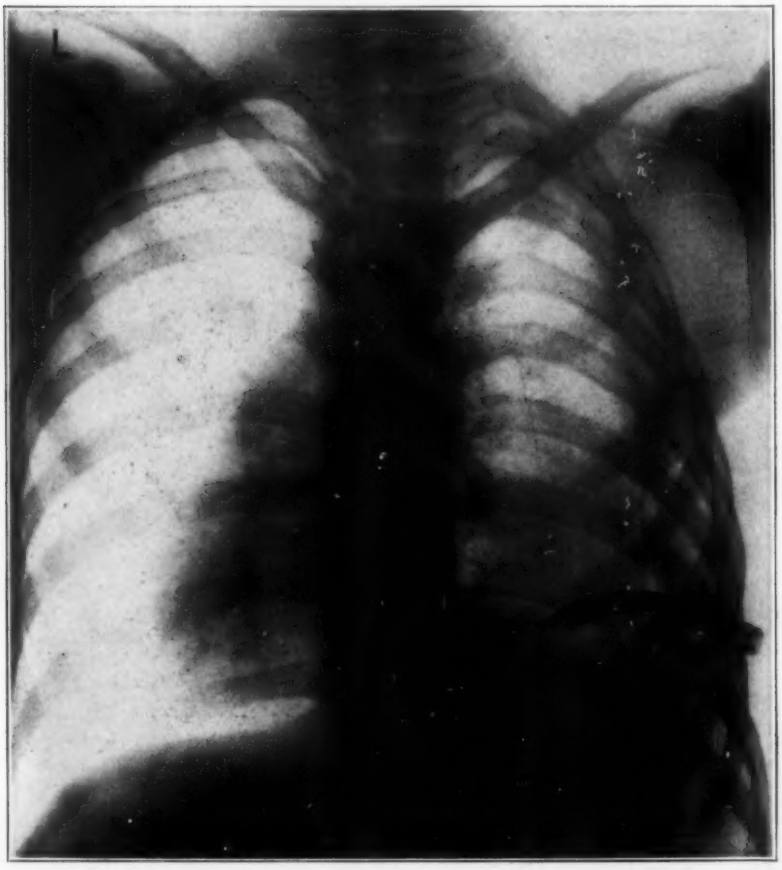

Fig. 7.—Same chest as shown in figure 6, after twenty-four days of treatment by continuous tidal irrigation and suction. The patient was ill, and following operation there was a sharp rise of temperature to 104 F., with a drop to 100 F. the following morning. There was immediate and constant improvement, the patient's temperature remaining around 99 F. to 100 F., with a few elevations explainable by severe abscesses over the back. At the time this picture was taken the cavity holds less than 8 cc., and a rapid healing is anticipated.

With this opening freely patent at all times, and with the continuous irrigation, the drainage must be as good as, if not better than, with a rib resection and a larger opening.

Not the least of the advantages is the interest which the patient manifests in the irrigation. This applies equally to the child, who is proud of the apparatus and treats it like a toy, watching the motion of the fluid and the particles of pus darting back and forth, and to the adult, who on seeing flakes of fibrin in the tube moving with the tidal flow, will deliberately, with a long and forced expiration, force them into the bag, where they settle down to the bottom and are eventually siphoned off to the drainage bottle.

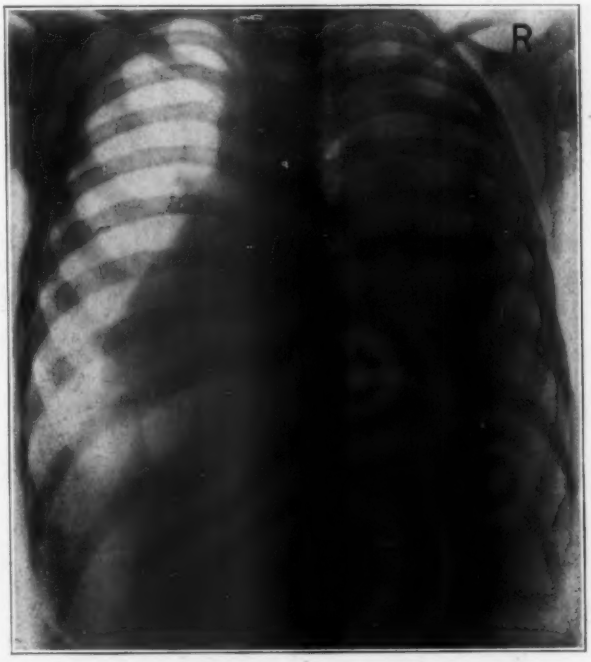

Fig. 8.—Chest of a boy, aged 5, with a pneumococcus, type IV, empyema. The history suggested the onset with pneumonia for a week, followed by the empyema, which had been present for five weeks. Over this period there had been pain in the chest, high fever, sweats, and a progressively down hill course.

ACUTE EMPYEMA COMPLICATED BY BRONCHIAL FISTULA

In cases of acute empyema with a bronchial fistula in which the patient did not cough up the pus from the cavity, irrigation was tried. If, as frequently happened, this did not produce irritation and coughing, the irrigation apparatus shown in figures 1, 2 and 3 was used. This proved to be unsatisfactory, however, since the continual leakage of air into the empyema cavity soon filled the rubber bag with air until it was under marked pressure. There must of necessity have been some associated compression of the lung where the empyema was acute and the

cavity not surrounded by dense scar tissue. With the tube to the drainage bottle open, there was still considerable pressure within the rubber bag, and this could not be relieved until the drainage tube was emptied of fluid and its lower end raised above the level of the fluid in the drainage bottle.

To overcome this complication, the apparatus illustrated in figure 10 was devised. This consists of a flask partially filled with irrigating fluid, connected by an opening at its dependent part to a short tube entering the empyema cavity. An irrigation bottle is connected to an opening at the top of the flask, while through a cork is passed a tube opening to

Fig. 9.—Same chest as in figure 8 after forty-eight hours of treatment with continuous tidal irrigation. The pus was thick, but the tidal flow was perfectly satisfactory for the first fifteen hours.

Apparently at that time the lung had expanded sufficiently to permit of the two pleural surfaces rubbing together with the respiratory movements, and the shaggy exudate over the surface was dislodged. As soon as this was removed from the empyema cavity by manipulating the tube and by frequent irrigations, there was no further embarrassment to the free flow of the tidal irrigation, and there have been no other large masses of fibrin.

In the early morning at the time of the freeing of the large amount of fibrin and exudate, the patient's temperature was 104 F. However, forty-eight hours after the thoracotomy was performed, the temperature remained below 100 F. for the entire day.

As far as could be determined at that time, there was only a small amount of fluid within the empyema cavity.

the outside air, and a siphon extending from the bottom of the flask to a drainage bottle. The tube to the irrigation flask is closed by clamp *a*, the siphon by clamp *b*, and the vent to the air can be closed when desired by clamp *c*. The apparatus is worked entirely like that shown in figure 1, except that with the rigid-walled flask the vent to the outside air must be left open. This, however, provides for the immediate escape of any air

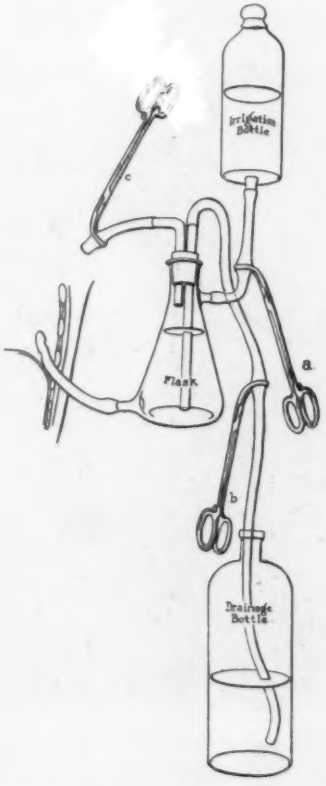

Fig. 10.—Diagrammatic drawing of the apparatus used in the cases of acute empyema with a bronchial fistula. There is a tidal irrigation between the empyema cavity and the flask. The clamp *c* is removed the greater part of the time, so that there is free irrigation, and any air entering the flask escapes readily through the vent. This apparatus also permits, by removal of clamp *b*, the siphoning off of the fluid within the flask, except for a small amount at the bottom. The flask is refilled by removal of clamp *a*. If it is desired to make suction on the empyema cavity with the flask partially filled, clamp *c* is applied and clamp *b* removed, thus giving a negative pressure within the flask. After the bronchial fistula closes, this apparatus is replaced by that shown in figures 1, 2 and 3.

which enters the system from a bronchial fistula. In replenishing the irrigation fluid, care must be taken not to siphon off the fluid to such a level as to permit air to enter the siphon. If this happens, however, no

harm comes from the entrance of air into the chest, since it is continually coming in through the bronchial fistula, while if the siphoning action is destroyed by air entering the tube, it is readily reestablished by closing clamp *c*, clamping off the tube to the empyema cavity, and opening clamps *a* and *b*. Suction can be applied as desired by closing clamp *c* with the flask relatively full, and opening the siphon on a closed cavity by removal of clamp *b*. By this means it can be determined when the fistula is closed, suction can be used as desired, and after it is proved

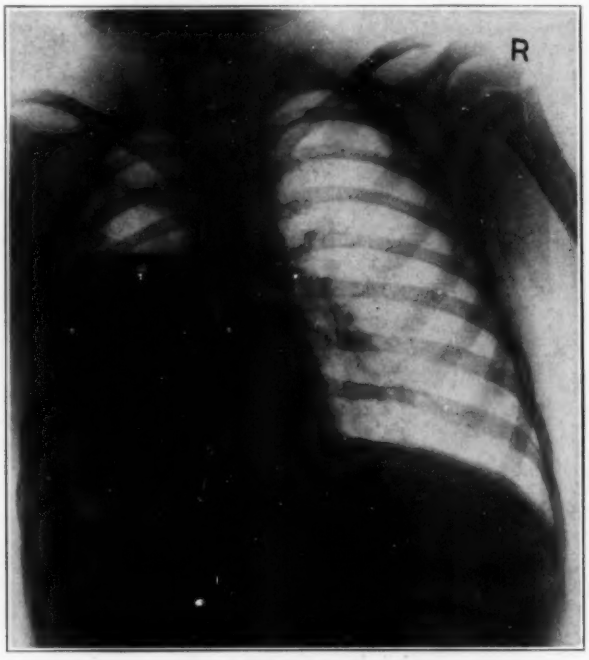

Fig. 11.—Chest of a girl, aged 5, with an acute pyopneumothorax of unknown duration, just before a trocar thoracotomy was performed. A bronchial fistula was present, and the cavity was treated by continuous tidal irrigation, using the apparatus shown in figure 10. The temperature dropped to normal and remained below 100 F. for the postoperative course.

that there is no further leak, the case can be treated like a simple empyema.

This apparatus is to a certain extent cumbersome, and demands rather careful adjustment; the flask cannot be completely emptied, and the opening to the chest is near the bottom of the flask where the thicker pus collects. However, it has proved satisfactory in the cases in which it was used. It seems likely that it will be desirable to replace it by a rubber bag, which provides for the ready escape of the air which enters from the bronchial fistula.

With the use of the flask there is the least limitation to the movements of the patient and the minimal traction on the tube entering the chest; and every possibility of spilling the irrigation solution in bed is avoided by suspending the flask from an overhead frame so that it just clears the bed and normally hangs immediately adjacent to the thoracotomy opening.

SUMMARY

A method is described with illustrations of the apparatus used in treating patients who have acute empyema, with or without the complication of a bronchial fistula, by continuous tidal irrigation carried on by the normal respiratory movements.

The trocar thoracotomy subjects the patient to the minimal operative procedure.

As the irrigation tube practically never becomes plugged, there is no obstruction to free drainage. In addition, the cavity is being continually washed out by relatively clean solution, so that there is more efficient cleansing and drainage than with the rib resection and open thoracotomy.

There is not the large raw surface to become infected by the continual soiling at the time of and following operation.

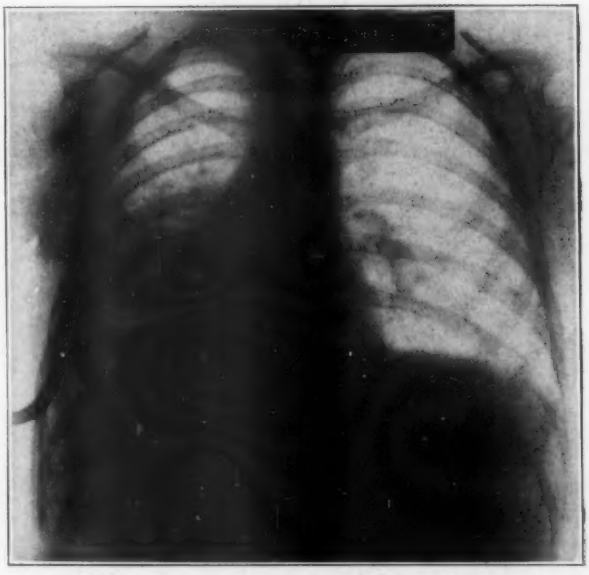

Fig. 12.—Same chest as figure 11, taken on the thirteenth postoperative day. At this time the tidal irrigation system ceased to work, and on attempting to open the tube it was found that there was no cavity, but only a sinus the size of the rubber tube. The patient is apparently well, free from pain, and playing, with a normal temperature and practically no drainage from the sinus.

There is only late and negligible leakage around the tube in the thoracotomy wound, so that dissecting infections do not occur, and dressings are practically eliminated.

Suction can be applied as desired, even as long as from six to eight weeks after operation, when expansion of the lung is slow after long compression. Even then there is little if any leakage of air around the tube in the thoracotomy wound.

The apparatus used in the presence of a bronchial fistula permits the immediate escape of air from the drainage system without the possibility of the air reentering the chest or disturbing the siphoning action.

By this method of treatment, the closing of the empyema cavity is more rapid than by the early institution of rib resection and open drainage.

EPITHELIAL NEOPLASMS OF PERIPHERAL AND CRANIAL NERVES

REPORT OF THREE CASES; REVIEW OF THE LITERATURE

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I wish to record three interesting cases of tumors of the nerve.

The first case is one of an epithelial neoplasm of the median nerve which recurred after excision, but which did not metastasize to distant organs. This case was associated with von Recklinghausen's disease.

The second case is one of an epithelial neoplasm of the radial (musculospiral) nerve which recurred and metastasized to other nerves. This case was associated with malignant neoplasms of the lung, liver, heart, brain, dura, calvarium and suprarenals.

The third case is one of an encapsulated tumor of the spinal accessory nerve.

EPITHELIAL NEOPLASM OF THE MEDIAN NERVE ASSOCIATED WITH RECKLINGHAUSEN'S DISEASE

CASE 1.—*History.*—Mr. J. C., aged 35, complained of pain in the right shoulder extending down to his hand for the preceding six months. The patient said that the pain followed a sudden strain in the raising of sacks of flour.

Following the accident, he was not immediately incapacitated. The arm did not swell immediately, nor was any evidence of ecchymosis noted. He said that the pain became progressively more acute and was associated with marked loss of muscle power, evidenced by the inability to raise heavy packages as he was accustomed to do.

The patient presented evidence of von Recklinghausen's disease (multiple neurofibromatosis). The right forearm was smaller than the left, and the carrying angle was diminished. There was limitation of extension of the elbow, but no limitation of flexion, pronation or supination. There was marked atrophy of the thenar muscles, as well as of the muscles of the palm of the hand. The skin was glossy over the right hand, and the fingers showed marked difference in color, with hyperesthesia of the index and middle fingers and thumb. On the inner aspect of the right arm, about 2 inches (5 cm.) above the internal condyle, there was a mass which extended down to the level of the internal condyle and in front of it to a point corresponding to the level of the insertion of the biceps muscle. This mass was hard and tender to the touch, but not adherent to the skin. The tumor was slightly movable, did not pulsate and was apparently definitely localized on the inner aspect of the biceps muscle.

He was advised to have the mass removed, as it was thought the condition was a neuroma of the median nerve. The patient was told that without removal, the condition would probably become worse, but it was impossible to assure him that he would have complete return of muscle power as a result of the operation.

Operation.—June 12, 1922: The operation was performed by me with Drs. Woodruff and Lutterloh assisting. Ether anethesia was given by Dr. Allgeyer. A preanesthetic hypodermic injection of one-fourth grain (0.016 Gm.) of morphine and one one hundred and fiftieth grain (0.0019 Gm.) of atropine was given. The anesthetic was started at 10: 47 a. m., and discontinued at 12: 06. The operation was started at 11 and was discontinued at 12: 12, the procedure consisting of excision of the neuroma and transplantation of the median nerve into the ulnar nerve in the right arm.

An incision about 3½ inches (8.87 cm.) long was made on the inner side of the biceps muscle corresponding to the course of the brachial artery. As soon as the soft tissue was dissected away and the muscles retracted, the large mass with the blood vessels came into view. The median nerve was isolated above the level of the tumor and a pair of forceps insinuated between the brachial artery and the median nerve to act as a support. After this the dissection of the tumor, which was continuous with the median nerve, was carried on, and the mass entirely separated from the brachial artery. It was shown to be a spindle-shaped mass about 2½ inches (6.27 cm.) in its long axis and ¾ inch (1.9 cm.) transversely. In one place on the outer aspect of the mass, it had broken through as

Fig. 1 (case 1).—Gross specimen of tumor of median nerve.

though there had been a slight hemorrhage. The lower limit of the tumor was just above the bicipital fascia (fig. 1).

Procaine hydrochloride was injected into the median nerve above the level of the neuroma, and a section was made of the nerve above. Then the nerve was sectioned below. This left a distinct gap of about 3½ inches. It was impossible to consider elongation of the nerve to close the defect, and therefore the question of where to graft the distal end was considered. It was decided to utilize the ulnar nerve. This was exposed behind the internal condyle and isolated and mobilized. A tunnel was made under the pronator teres with a pair of forceps. The distal end of the median nerve was brought under the tunnel and grafted into the lateral aspect of the ulna with fine silk. The proximal end of the nerve, which was cut instead of being left unattached, was sutured to the internal cutaneous nerve, which was exposed in the wound. The wound was sutured in tiers with fine catgut to approximate the muscle and subcutaneous tissue. Michel's clips were used for the skin. Cross-section of the tumor showed that it contained a good deal of connective tissue and some degenerating areas which looked like colloidal material. A diagnosis of neuromyxosarcoma was made.

Laboratory examination showed a somewhat cylindric-shaped structure measuring 7 cm. in length and 3 cm. at its broadest diameter. It tapered at each

extremity, which was seen to be made up of a number of individual cords or fibers held together by an enclosing connective tissue, and appeared to be a nerve trunk which had been ballooned out by a growth within, causing stretching, and in one place, rupture of its sheath. It was almost uniform throughout, except about its upper third, where there was a dark reddish-brown mass, 2 cm. in thickness, projecting outward for about 1 cm. beyond the surface of the main growth. The specimen was for the most part reddish brown, with the exception of the foregoing protuberance, which was somewhat darker. It was firm but here and there a few nodules could be detected. On sectioning, it offered some resistance to the knife and presented a cut surface which was made up entirely of a new growth that had replaced the nerve tissue, the fibers of which were apparently at each extremity. No nerve bundles were noted on gross study. The cut surface of

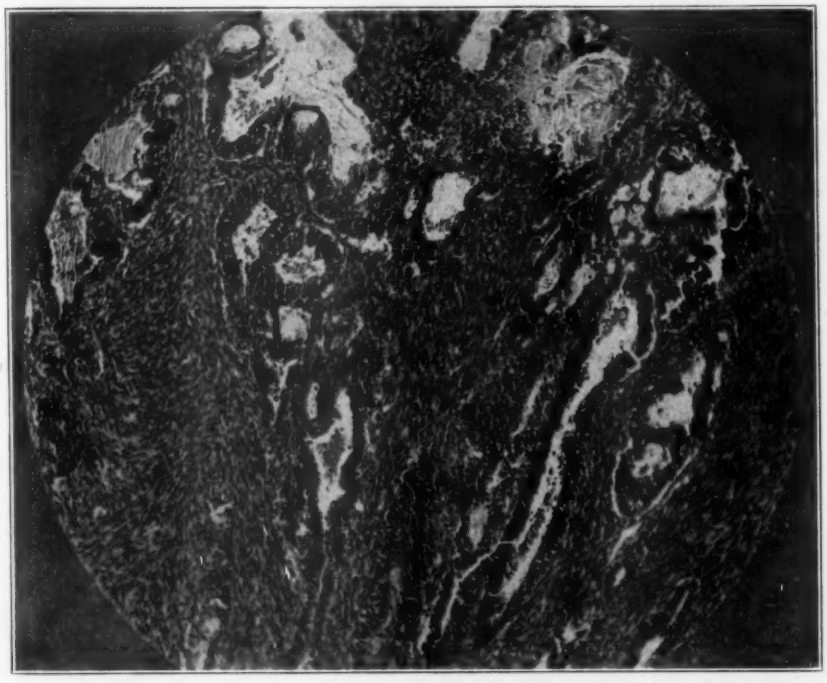


Fig. 2 (case 1).—High power magnification of primary growth.

the main mass was made up of a number of irregular lobulations divided by a stroma into areas of varying sizes and more cellular appearance, resembling gland spaces. It was rather translucent, giving somewhat the appearance of a myxomatous type of tissue. Some of these areas appeared to be necrosed, as was evidenced by increased friability and a dirty yellow color. The structure resembled carcinoma that was growing fairly rapidly. The cut surface of the more rapidly growing mass, which appeared to have ruptured through the covering membrane of the main growth, was uniformly reddish brown and cellular. The blood vessels were not prominent.

Histologically, on first sight the tumor closely resembled carcinoma; a number of glandlike spaces cut in several directions were noted, some being circular and others long and rather tortuous, surrounded by a supporting structure of varying character and degrees of density. The larger gland spaces contained an amorphous

structure-like material. They were lined with cells that were tall and columnar in their general appearance, which were closely packed together, and on close study showed practically no separation of the individual cells; the appearance was that of a multinucleated syncytial mass resting on an underlying structure resembling a basement membrane. The entire glandular structure was divided into areas of various sizes by a cellular supportive material showing nuclei occupying a relatively large proportion of the cell; there was a minimum amount of intercellular substance. Most of the supportive structure was suggestive of nerve tissue, but I was unable to find positive evidence of a former nerve trunk anywhere except on the periphery. Mitotic figures were noted both in the epithelial and supportive cells. The blood supply of the part was not prominent, the vessels being present in stroma. A few areas of necrosis and degeneration were noted, but these were confined largely to the glandlike spaces. In some places, the stroma was myxomatous, and in others, it was made up of a denser tissue.

Fig. 3 (case 1).—High power magnification of first recurrence showing glandular elements.

A tentative diagnosis of carcinoma of the gland cell type was made, with the explanation that further study was required to determine definitely the primary origin (Lanford).

Progress Notes.—Following the operation, the patient had a sensation of pain and touch in the thumb and all fingers. He was able to flex and extend his wrist. Three days after operation, common sensation was noted in the peripheral distribution of the median nerve. The wound healed by primary intention. When the patient left the hospital ten days after the operation, common sensation was present as already noted.

During October, 1922, the patient returned, because a painful lump had developed in the upper portion of the wound caused by the previous operation. This was believed to be neuroma of the stump of the median nerve, and operation was advised.

Operation was performed on Nov. 3, 1922, by me, with the assistance of Dr. Sneed. Ether anesthesia was used and was given by Dr. Baker. The resection of a recurrent neoplasm was performed.

Second Operation.—An incision about 3 inches long was made, and the median nerve was exposed above the level of the tumor. The vessels were located and dissected away from the tumor. The nerve was injected with 80 per cent alcohol above the level of the tumor and sectioned. A large vessel in the center of the nerve had to be ligated, as it was not controlled by the injection. The stump was dropped back and the mass carefully dissected from the vessels and removed. The fascia and fat were approximated, after which the skin was closed, interrupted

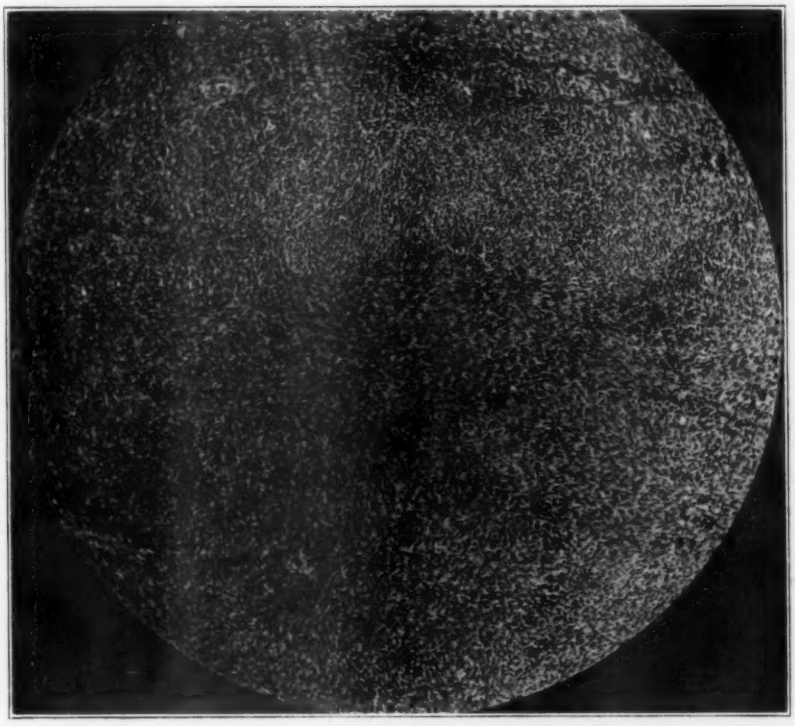


Fig. 4 (case 1).—High power magnification of solid portion of first recurrence.

sutures being used. The patient experienced little discomfort, and left the hospital two days later.

Laboratory examination was made of a small piece of tissue, measuring 3 by 2 cm., irregular in shape and presenting different degrees of density, one area being firm. Its outer surface was pinkish gray. The greater part of the cut surface was pinkish gray, but showed here and there a few areas with a dirty yellow necrotic appearance. In one place a more cellular structure was noted, which elevated itself above its surroundings when the mass was cut.

"Histological study shows a picture similar to the primary growth and a diagnosis of recurrent carcinoma of undetermined origin was made" (Lanford).

Progress Notes.—On June 23, 1923, the patient returned because of the development of a mass on the inner aspect of the elbow. Examination at this time revealed the following: The patient was well developed and did not show any evidence of emaciation. With the exception of the tumor mass at the elbow, nothing in his condition indicated general discomfort. The scar of the previous operation on the right arm was healthy. The elbow was flexed at a right angle. There was little mobility of the joint, and the forearm was midway between pronation and supination. Some atrophy of the muscles of the hand was present, but sensation of pain, touch and temperature in the forearm was undisturbed. However, there was some diminution of sensation in the index finger.

Dr. Holbrook, a neurologist, examined the patient and reported: "Sensation of pin and cotton is good over the palmar surface of the right hand, except in

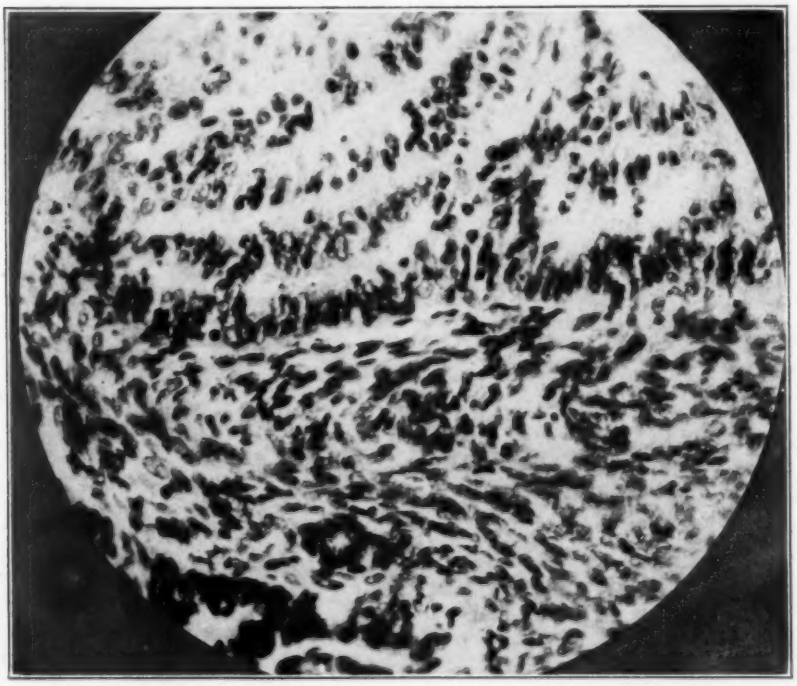


Fig. 5 (case 1).—High power magnification of first recurrence.

the index finger, in which sensation is dulled about the middle and beyond this point is absent. Thermal sensation is inaccurate over most of the hand, especially toward the index finger. Temperature differences are appreciated toward the center and inner side of the hand."

Third Operation.—On Jan. 25, 1923, I performed an operation with Drs. Macheca and Liles assisting. Dr. Allgeyer gave the ether anesthesia.

The amputation was made at the junction of the middle and upper thirds of the right arm. A tourniquet was applied, a circular skin flap dissected up, and the muscle cut at the level of skin retraction. The muscles were retracted and the humerus sawed through. The large nerves were then brought down into the field, and an inverted V-shaped excision of the end approximated the sheaths

with plain catgut, making a fish-tail appearance after the suggestion of Corner. The nerves were injected with 95 per cent alcohol following the suggestion of Carl Hoover and Lewis. The muscles were quilted over with plain catgut after ligation of the large vessels. Chromic catgut no. 2 was used for ligation. There was little bleeding. Interrupted plain catgut sutures were introduced into the sheath to diminish the amount of dead space. The skin was closed with silkworm and plain catgut interrupted sutures. The specimen was sent to the laboratory for preservation. Amputation was done because the removal of sufficient tissue to remove the entire mass would leave a useless arm.

A gross specimen was taken from an amputation of the lower third of the arm and forearm. The dissection was done by Dr. Lanford, and the line of the previous incision along the course of the ulnar nerve was incised. The skin

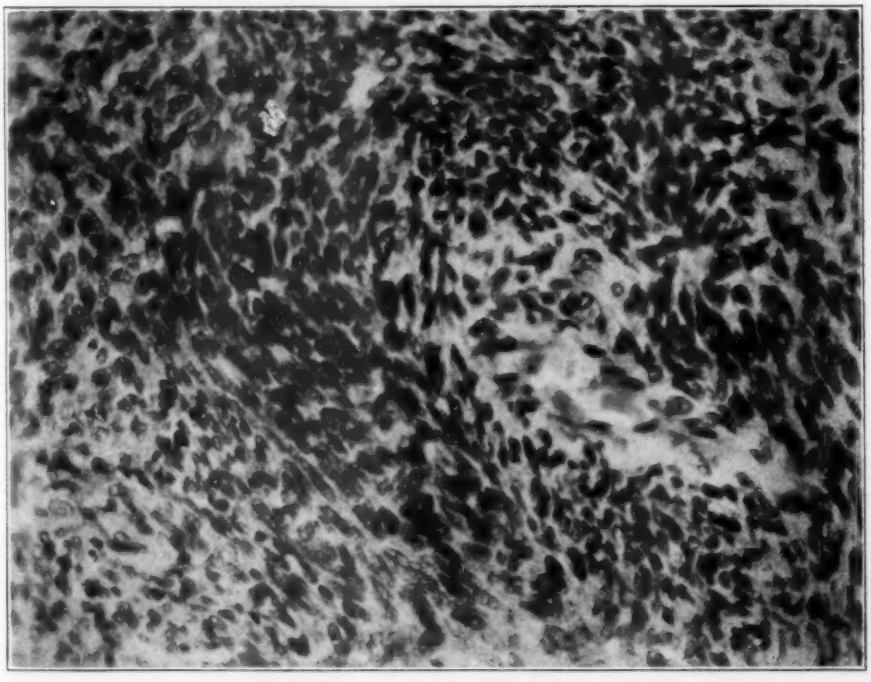


Fig. 6 (case 1).—High power magnification of first recurrence. The glandular elements are being crowded out by the embryonal character of the stroma cells.

and fat were retracted. The ulnar nerve, prior to its entry into the pronator teres, was exposed and the nerve followed down to a point where it was lost in the tumor mass just above the internal condyle. The skin flap was then dissected away from the muscle, exposing the biceps and the tumor mass, which was covered by the flexor muscle originating from the internal condyle. The brachial artery was then retracted medial to the ulnar side, exposing the median nerve below. We then followed the median nerve to its point of implantation into the ulna by cutting through the pronator teres and palmaris longus muscle bellies. We could see the suture line as evidenced by the black silk which had been used a year ago. There was apparently no thickening of the exposed portion of the

median nerve at its anastomosis with the ulna. The belly of the flexor sublimis digitorum was ballooned out by the growth and gave the appearance of a funnel. In order to disturb the appearance as little as possible, Dr. Lanford took a small block of the tumor out of the ballooned portion of the palmaris longus belly. This was then sutured in order to retain the contour of the original growth.

Laboratory examination showed a specimen made up of the forearm and hand and about 6 inches (15.24 cm.) of the arm, which presented a tumor involving the structures at the bend of the elbow. In gross, the hand showed considerable atrophy changes, but otherwise was normal. A marked swelling was noted mostly at the bend of the elbow on the anterior surface, extending backward and laterally to involve most of the structures. The overlying skin was intact and loose over the growth, and there was a long, well healed scar from a former

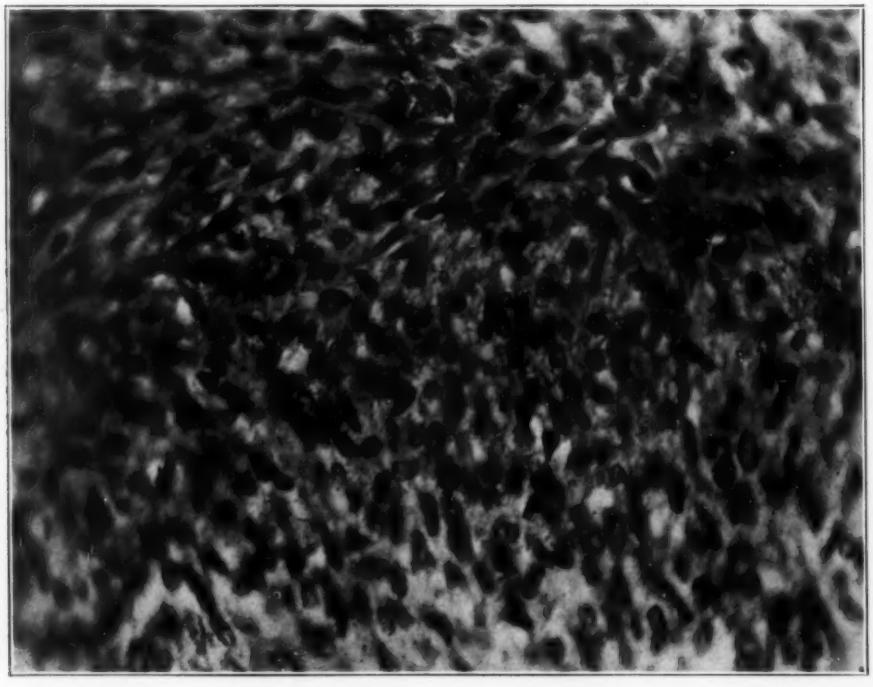


Fig. 7 (case 1).—High power magnification of second recurrence.

operative procedure. When the skin was dissected back, a new growth was found that had involved the muscles of the part, particularly all those inserted into the internal condyle of the humerus, and to a lesser degree those of the external condyle. The muscles were pushed upward and were thinned out, this being particularly noticeable in the superficial layer, while the deeper layer was more infiltrated and replaced by the main growth. The main mass was 11 cm. in length and 8 cm. at its thickest portion; it was roughly cylindric or funnel-shaped, the upper portion being at the bend of the elbow, and the pointed end extending onto the forearm. It was firm, and here and there presented nodulations which were smooth and were firmly adherent to the overlying muscle. On sectioning, it offered considerable resistance to the knife and presented a cut surface that was

grayish white and apparently made up largely of supportive tissue. The bands of tissue running in all directions gave somewhat the appearance of a leiomyoma of the uterus. The blood vessels were not prominent, and only here and there were areas noted which appeared to be well supplied with blood. An occasional area on the cut surface was noted which showed degeneration suggestive of a myxomatous or loose, meshlike type of structure containing a clear pinkish stained serum, but no definite lobulation or cystic cavity could be found.

Microscopic study showed the mass to be almost uniformly made up of spindle-shaped cells running in bundles in all directions. Some of these strands were considerably older than others and tended to separate the more rapidly growing ones into distinct areas. Here and there little microscopic cavities could be noted

Fig. 8 (case 1).—Patient several months after amputation.

that were lined with a single layer of cells resembling epithelium. The blood vessels were not prominent in the main portion, although here and there a few capillaries were noted. Some of the older portions of the growth showed considerable deposition of collagen-like material, and still others were somewhat myxomatous. Many of the cells were rapidly growing and showed mitotic figures. The histology was that of a neurogenic sarcoma, with absence of the glandlike spaces noted in the primary growth.

Progress Notes.—On June 29, the wound was dressed. Swelling was not noted, primary union occurred and the patient was permitted to go home, but was kept under observation for more than a year. His general condition continued good, with no evidence of recurrence or development of the tumor in any other location.

When last heard from, four years after operation, he weighed 200 pounds (90.7 Kg.) and was in excellent health.

Summary.—1. A patient with von Recklinghausen's disease presented a tumor of a peripheral nerve.

2. The tumor resembled a carcinoma. It was made up of glandlike spaces lined by columnar cells with little separation of the individual cells, which gave the appearance of a syncytial mass. Mitoses were noted.

3. After excision of the tumor, recurrence occurred in the stump.

4. Histologically, this resembled the primary tumor.

5. A second recurrence necessitated amputation.

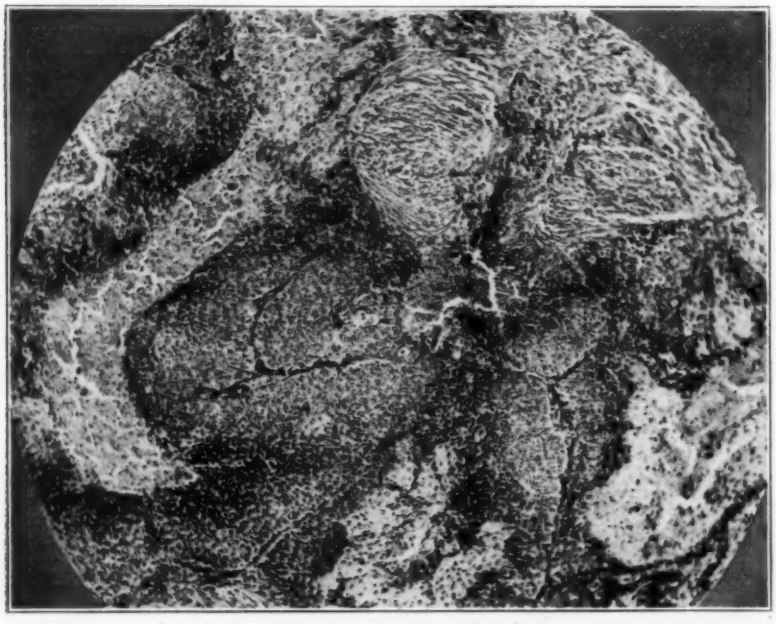


Fig. 9.—Low power magnification of first recurrence tumor of the radial nerve.

6. This tumor contained spindle-shaped cells. There were small cavities which were lined with a single layer of cells resembling epithelium.

7. The patient remained well for at least four and one-half years. Since that time, we have been unable to trace him.

8. The tumor was epithelial.

9. It caused expansion of the nerve and disturbance of the peripheral distribution of the nerve.

10. There were no distant metastases.

Certain questions naturally arise: 1. What is the origin of a tumor of the nerve which is epithelial? 2. Is it part of a systemic disease? 3. What is its relation to von Recklinghausen's disease? 4. Did it come

from a misplaced cell rest or can it be explained by referring to the histogenesis of some element of nerve tissue?

Tumors of the peripheral nerve must originate (1) from some constituent of the nerve; (2) from misplaced cells; (3) be part of a systemic disease, or (4) be metastatic growths.

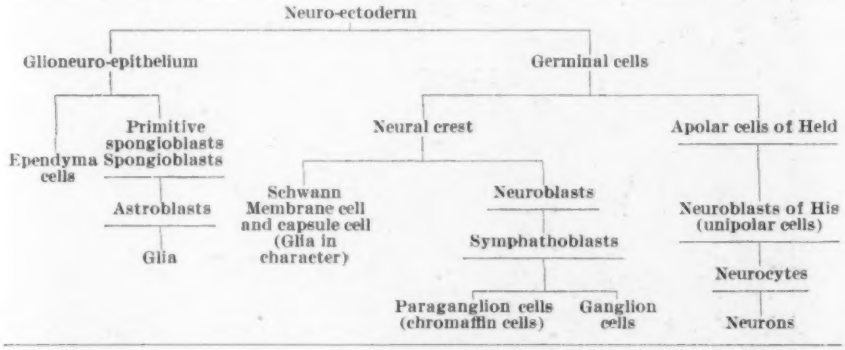
To develop the subject, it will be necessary to introduce a brief review of the embryology of the nervous system and the facts as well as the theories available in the literature.

Some of the following data are essentially academic, but necessary to present the subject clearly.

Embryology.—According to Hardesty: [1]

The essential elements of the nervous system, the nerve cell-bodies and the essential portion of all nerve fibers, central craniospinal and sympathetic, develop from one of the embryonic germ layers, the ectoderm, and all arise from a given

Histogenesis of Nervous System (Glober and Strauss)



region of that layer. Further a small portion of the supporting tissue of the nervous system the neuroglia, is of the same origin.

Peripheral Nerves.—According to Stookey: [2]

A typical peripheral nerve is made up of neuraxes from nerve cells either within the brain stem and spinal cord, or from cells of the spinal, cranial and sympathetic ganglia.

Two main theories have been offered concerning the origin of the neuraxes, one the outgrowth theory of His (1890) and the other the cell chain theory of Bethe (1903) and others. A still older theory is that of Henson, according to which there always are protoplasmic intercellular bridges in the developing embryo and out of certain of these bridges the nerve fiber is differentiated. Held (1909) has supported a modification of this theory, according to him the nerve fibers differentiate from the nerve cell bodies along these protoplasmic bridges.

1. Hardesty, Irving: The Development of the Nervous System, in Morris' Human Anatomy, Philadelphia, P. Blakiston's Son & Company, p. 754.

2. Stookey, Byron: Surgical and Mechanical Treatment of the Peripheral Nerves, Philadelphia, W. B. Saunders Company, 1922.

After twenty years of experimental observations (1904-1924), Harrison [3] stated:

One who follows historically the subject of the histogenesis of the nervous system cannot but be impressed by the deviousness of the path of progress.

With the foundation of the neuron theory by His (1886) and Forel (1887) the study of the nervous system entered upon its modern phase.

The investigation of His (1886, 1887, 1888, 1890) followed by the work of Ramon y Cajal (1890, 1892, 1894), who first applied the Golgi method to the study of the embryonic nervous system, and that of v. Lenhossek (1892, 1895), gave a firm footing to the concept of the neuron by showing clearly, as it then seemed, that each fiber arises as the outgrowths of the single ganglion cell.

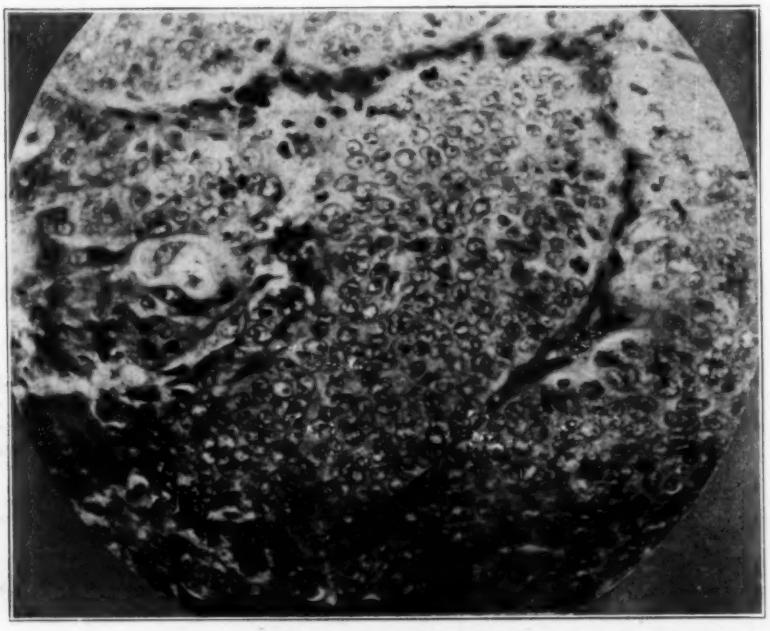


Fig. 10.—High power magnification of first recurrence.

Experiments, with hanging-drop cultures of embryonic nervous tissue in clotted lymph, rendered possible the direct observation of the growing nerve fiber, showing the latter to be not a chain of cells, but a strand of hyaline protoplasm with an active amoeboid end, through the motion of which the fiber is spun. In other words, it was actually seen that nerve fibers grow as the process of a single neuroblast.

To sum up the impression gained from the study of the relevant literature accumulated since 1900, we find that the neuron concept, so far as it applied to the development and regeneration of the nervous system, remains unshaken under the attacks it has received, and that it now stands more firmly established than ever.

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3. Harrison, Ross G.: Neuroblast Versus Sheath Cell in the Development of Peripheral Nerves, J. Comp. Neurol. **37**:123 (June) 1924.

The problem before us is, simply how the axon is constituted in development —whether it takes origin from a cell chain, or is the process of a single ganglion cell.

The method of procedure was to eliminate by appropriate operation first the source of the sheath cells, and, second, that of the motor ganglion cells.

The development of the axon is a function of the neuroblast.

The removal of any body of neuroblasts invariably results in the elimination of the peripheral nerves normally connected with them.

I may therefore proceed with the study of the development of the peripheral nerves, accepting as a proved fact that the neuraxis or axon is a product of the neuroblast, and continue to construct my concep-

Fig. 11.—Dissection of amputated limb.

tion of the development of the remaining portions of the peripheral nerve.

According to Stookey:

The neuraxis extended without interruption from the cell of origin to its ultimate termination. It consists of neurofibrils imbedded in a semifluid neuroplasm and surrounded by a very delicate membrane, the axolemma. The fibers are described as of two types, medullated, and nonmedullated, depending upon the presence or absence of a sheath known as a medullary or myelin sheath. The medullary sheath contains myelin—a chemical substance made up largely of lecithin, and supported by a framework or neurokeratin. Outside of the myelin is a delicate nucleated sheath known as the sheath of Schwann or neurolemma. The nonmedullated fibers of the peripheral nerves arise from the cells of the sympathetic and spinal ganglia.

Both medullated and nonmedullated fibers are assembled in nerve bundles called funiculi, and the funiculi in turn are joined together into a larger group by a surrounding sheath of connective tissue called epineurium, thus forming a peripheral nerve. The individual fibers of the funiculi are separated by a small amount of connective tissue called endoneurium and the funiculi are surrounded by a lamillated layer of fibrous tissue which encircles the funiculi, called by Key and Retziuz (1873) perineurium.

The origin of the cells of the sheath of Schwann has been a cause of great controversies.

Fig. 12.—Upper surface of dura.

Two main views have been held concerning the origin of these cells it being formerly thought that the sheath was of mesodermal origin. The more recent view on the other hand has been that the sheath cells were closely related to neuroglia and were of ectodermal.

The latter theory has been proved by Harrison's ganglion excision experiments.

By excising the ganglionic crest of young amphibian embryos peripheral motor nerves, in the form of naked axis cylinders, developed in place of nerves which normally had numerous spindle shaped sheath cells about them.

The experiments leading to this conclusion have recently been repeated by Muller and Ingver (1921) with like results.

Harrison said:

The sheath cells are best interpreted as a sort of peripheral neuroglia—an idea that has found favor with a number of students of the structure and development of the nervous system.

The sheath cells are clearly separated elements, which are closely applied to the axons. While they have but a small amount of cytoplasm, they are in no sense mere nuclei and part of the axon itself.

It is likewise definitely shown that the sheath cells are not mesodermal, but arise for the most part from the ganglion crest in connection with the spinal ganglia. Some arise later directly from the medullary cord by emigration along the ventral roots.

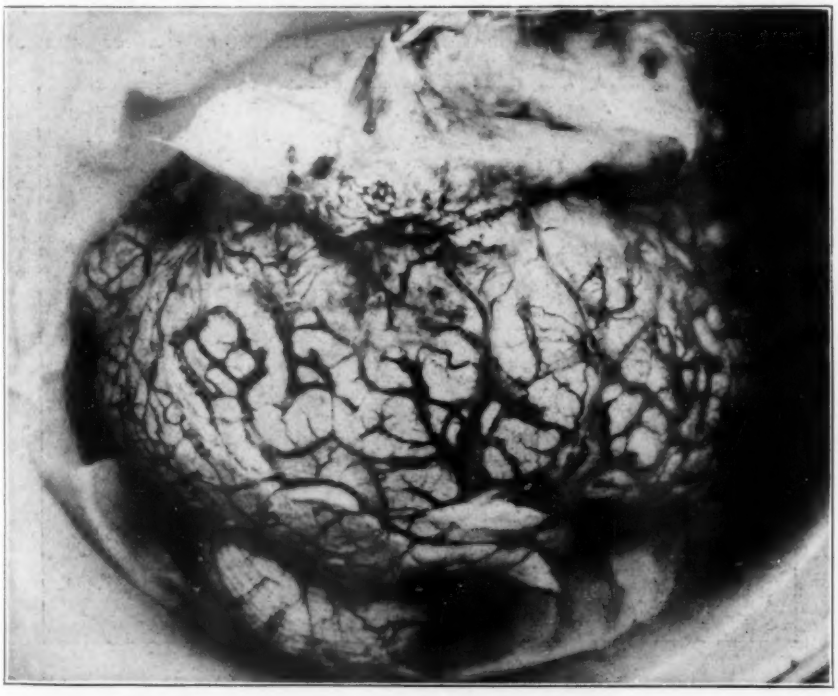

Fig. 13.—Gross photograph of brain with dura reflected showing neoplasm pressing on cerebrum.

The sheath cells are to be regarded as the neuroglia of the peripheral nerves.

The literature makes one feel justified in accepting the ectodermal origin of the cells of the sheath of Schwann.

When one turns to clinical experiences, one finds a state of confusion. If Harrison's work is correct, this confusion should cease to exist.

Pathology.—Is it possible for an epithelial recurring type of tumor of a peripheral nerve to arise from the elements of peripheral nerve, and may it be a part of a systemic disease, or must it be of metastatic origin?

Review of the literature is necessary to answer this question.

That this is a difficult question to answer can be appreciated by referring to Ewing:[4]

> Tumors of the peripheral nervous system form a very important complex group of neoplasms of frequent and varied clinical course.
>
> A satisfactory classification of these tumors is difficult, owing to the complex structure of the nerve trunks, and the uncertainty of the source of the supporting cells which accompany nerve fibers, such as the cells of the sheath of Schwann, the neurilemma, the endoneurium, and the lymph sheaths of nerve trunks, all of which participate in tumor growth.

Since the tumor in question occurred in association with von Recklinghausen's disease, it is only fair to determine whether such an

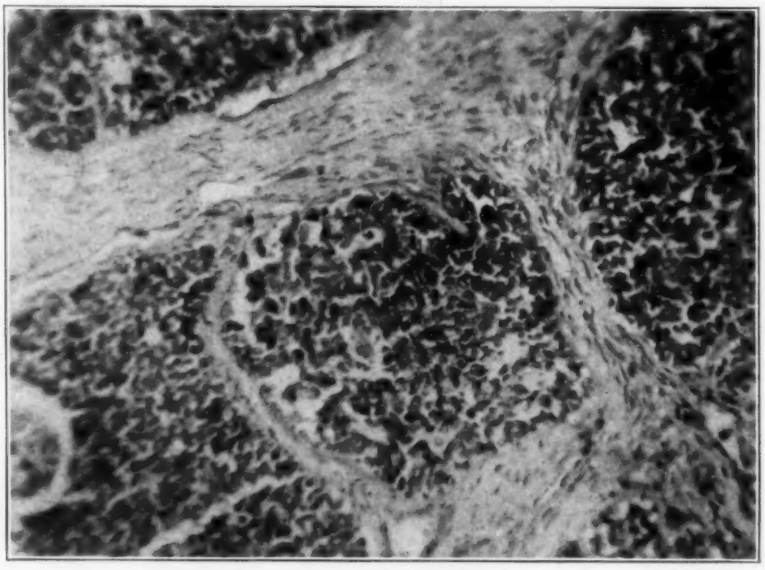

Fig. 14.—Low power magnification of tumor in dura.

association is within the range of possibility before attempting to explain it on another basis.

The problem which confronts one today confronted that illustrious master, J. Bland-Sutton[5] (1900), who said:

> In 1894 I published a book on tumors, and during its preparation I was sorely puzzled how to classify the tumors known as neuromata and fibromata, notwith-

4. Ewing, James: Neoplastic Diseases, Neurofibromatosis, Philadelphia, W. B. Saunders Company, 1922.

5. Bland-Sutton, J.: On Neuromata and Allied Conditions of the Skin and Nervous System, Clin. J., June, 1900, vol. 16.

standing the fact that Professor Recklinghausen had shown the pathological association of discrete molluscum and multiple neuromata.

Sutton defines a neuroma as "a tumor growing from and in structure resembling the sheath of a nerve."

"The tumors which most strictly correspond to my definition are those known as neuro-fibromata."

After discussing six apparently diverse conditions, such as neuromas, ganglionic neuroma, plexiform neuroma, molluscum fibrosum in its solitary as well as its pendulous and nodular forms, sarcoma of nerve and glioma of the central nervous system and its prolongations, he says they "are all due to a common cause, overgrowth of the delicate

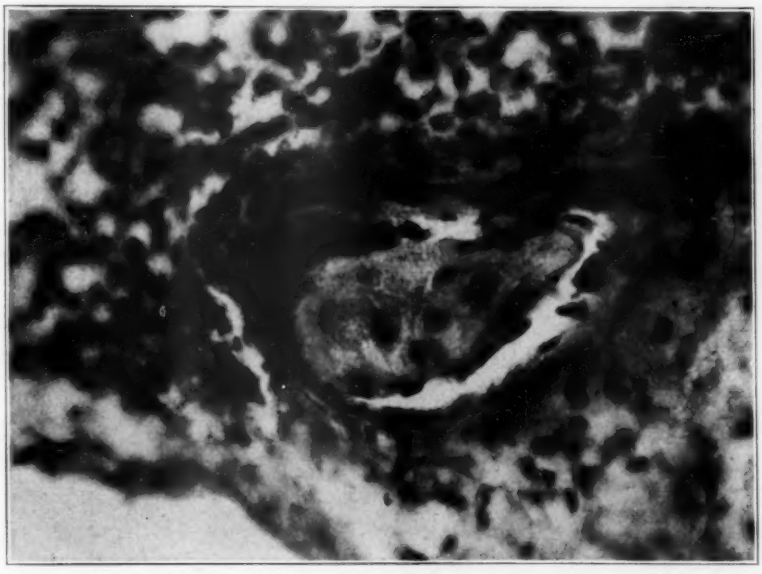

Fig. 15.—Metastasis to calvarium; high power magnification.

connective tissue which immediately surrounds the true nerve elements, the manifestation depending upon the particular part of the nervous system affected, the brain, spinal cord, large nerve trunks, terminal nerves in the skin or the delicate sustentacular framework of the retina."

These observations of Sutton are in harmony with those of Alexis Thomson, of whose monograph Sutton said: "No work equal to it in importance in relation to neuromata has appeared since Smith's" (1849, Dublin).

Thus the foregoing quotations show the view of the leading English authorities of the late nineteenth and early twentieth century.

The outstanding point today is the origin of the "connective tissue which immediately surrounds the nerve elements." Is he referring to the sheath of Schwann? That the type of cell which is its progenitor is ectodermal has apparently been settled by the experimental work of Harrison.

In 1908, Verocay [6] studied a specimen from a case in which he had performed the autopsy. The case presented "multiple tumors in the central nervous system and its meninges as well as in the course of the peripheral nerves." He presented the case hoping that it may help in

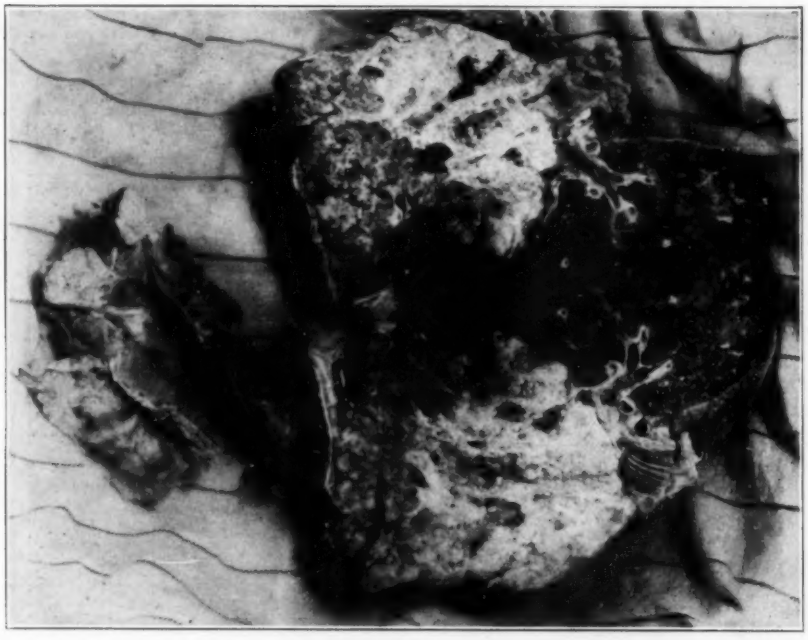

Fig. 16.—Tumor involving entire right lung showing occlusion of bronchus.

this way to clear up a rather obscure field in the pathology of the nervous system.

His expectations have been more than realized, because all students of this subject refer to him as the first to express the idea of the association of peripheral and central nerve growths and the ectodermal origin of these peripheral tumors (sheath of Schwann).

He said:

> The old dispute over the nature of Schwann's cells has at present been settled by showing that they are of ectodermal origin and that they originate from the same anlage as the specific nerve cells-nerve cells and glia cells.

6. Verocay, Jose: Multiple Tumors as a System Disease of the Nervous System, Festschr. f. Hans. Chiari, 1908, pp. 378-415.

He summarized as follows:

The above case was an extensive system disease of the central and peripheral nervous system and its meninges in the form of the multiple tumors of the spinal cord and medulla oblongata (glioma) the nerves (originating from the nerve fiber cells and the connective tissue?) and meninges (endothelioma).

2. This system disease is with great probability to be attributed to a congenital anomaly of development.

3. Tumors of the nerves occur with the picture of "Neurofibromatosis" (fibromatosis-nervorum) or "True multiple neuromas which originate from the so-called nuclei of Schwann's sheath, for which reason they are to be regarded as nerve tumors.

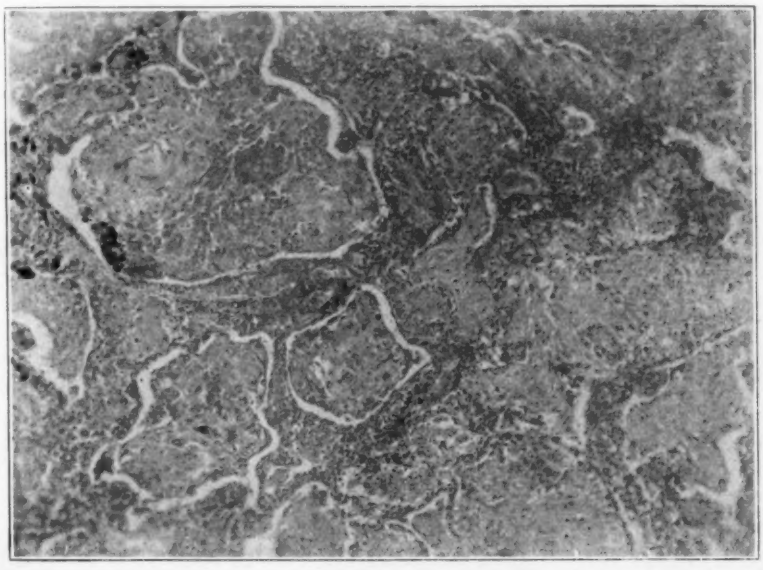

Fig. 17.—Low power magnification of tumor of lung.

4. These nerve tumors may also contain ganglion cells the presence of which seems to be most easily comprehensible if they are regarded as being derived from nerve fiber cells also in the normal development of the sympathetic.

Serre [7] presented two cases with peripheral tumors. He expresses the following positive opinions relative to several questions at issue in cases of tumors of peripheral nerves associated with Recklinghausen's disease: 1. These tumors originate from sheath of Schwann. 2. They are part of a systemic disease. 3. Von Recklinghausen's disease is not mesodermal in origin, but the tumors are "developed at the expense of the sheath of Schwann and hence are of ectodermal origin."

7. Serre, R.: Contributions to the Study of the Visceral Localization of Recklinghausen's Disease, Thesis, Paris, 1923.

Serre's paper must be freely abstracted:

The history of neurofibromatosis dates back to Recklinghausen who, in 1882, undertook the synthesis of the sparse findings in the previous observations of dermatologists, surgeons, and anatomo-pathologists.

The histologic conceptions of neurofibromatosis have varied greatly during the course of the last few years. After Virchow, who distinguished pure neuromas mixed neuromas (true neurofibromas) and false neuromas (fibro-myxomas, fibro-sarcomas), Recklinghausen, in 1882, grouped all the cases under the heading of fibromas.

To this purely connective conception in which the tumors were considered as being derived from the perineurium, Bard, in 1885, opposed a theory, sanctioned by Durant in which the neurofibroma was derived from the segmentary cell of the nerve fiber. With the investigations of Held and Nageotte on the histology

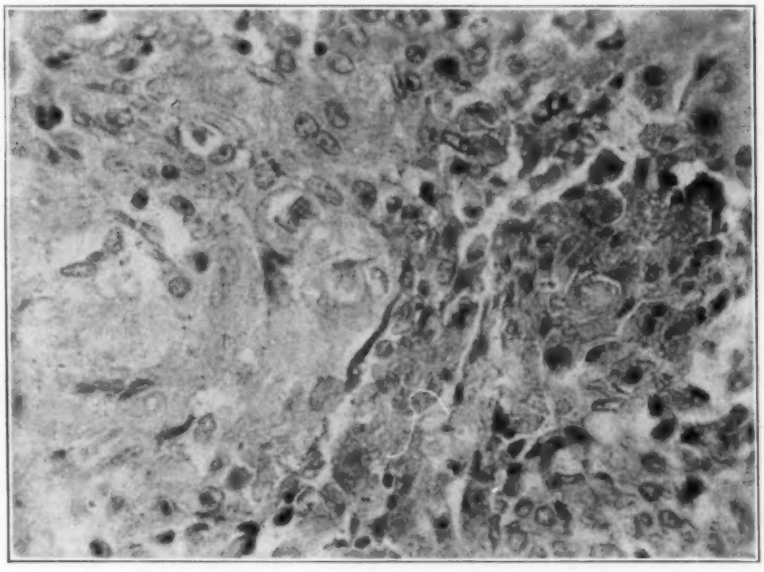

Fig. 18.—High power magnification of tumor of lung.

of the nerves and the works of Verocay, Trapier, Bard, Gall, Gautier, Delore, and especially with the recent studies of Lhermitte and Leroux, there has arisen the new theory of peripheral neurogliomatosis developing at the expense of the sheath of Schwann or the peripheral neuroglia.

Discussing Recklinghausen's disease, he said:

Lhermitte and Leroux state that the constitution of the peripheral tumors in Recklinghausen's disease has the fundamental characteristic of being formed by the combination of two tissues, one a compact tissue resulting from the juxtaposition of fusiform cells, the other more loose and reticulated formed of cells with ramifying protoplasmic expansions which anastomose together.

The compact tissue is formed of fusiform elements parallel to each other forming trabeculae, whorls and bundles. The cell itself has a regular ovoid

elongated nucleus surrounded by ill-defined protoplasm, separating the neighboring cells without cellular individualization, that is to say, the syncytial type. Finally a very important characteristic should be noted—the protoplasm is finely fibrillar.

The constitution of the reticulated tissue is very different from that of the compact tissue. Here the cellular elements are stellate cells with protoplasmic expansions more or less loose and anastomosing with the prolongations of the neighboring elements. The elements like the preceding, present a fibrillary protoplasm.

This general description seems to hold true for all the cutaneous and visceral peripheral nerve tumors of Recklinghausen's disease.

Nature of the Neoplastic Tissue.—Let us see now why these tumors may be mistaken for fibrous tumors of connective tissue origin and how they may be distinguished. There are three points to be considered: (1) the presence of

Fig. 19.—Tumor of heart and kidney.

collagen; (2) the morphologic appearance of the cells; (3) the disposition of the vessels.

Is collagen specific of connective tissue cells or vessels?

Up to the last few years it has been considered that the collagen framework of the connective tissue is an integral part of the connective tissue cell.

Lhermitte and Leroux have recently shown, in the case of an intra-ventricular echinococcic cyst, that there was precipitation of collagen in the middle of an adult neuroglia tissue.

In Recklinghausen's disease the presence of connective tissue cells cannot be concluded from the presence of collagen.

The morphological appearance of the cells is of capital importance. The cells of these tumors are formed of a protoplasm with indistinct outlines which is prolonged into a very fine fibrillary arborization anastomosing with the arborization of neighboring cells. Sometimes, even, the cytoplasm assumes a more clearly syncytial appearance and many clear nuclei may be found. Finally, under high magnification, the protoplasm is seen to be clearly fibrillar, this being

opposed to the appearance of clearly individualized adult connective tissue cells, the cytoplasm of which is never fibrillar.

These tumors in no way resemble fibroids from which they differ by the morphologic appearance of the cells, the vascular alterations and the necrotic areas.

Their cellular irregularities, their well individualized cells, the absence of vessels provided with true walls, their tendency to metastases, in a word, their characteristics of nonencapsulated malignant tumors differentiate them at once from the gliomas which are always encapsulated.

There is no point of equal contact between these peripheral tumors of Recklinghausen's disease and the connective tissue tumors. On the contrary there are four arguments which speak in favor of the neuroglial origin of these tumors.

1. The absence of cellular individualization, the syncytial appearance.

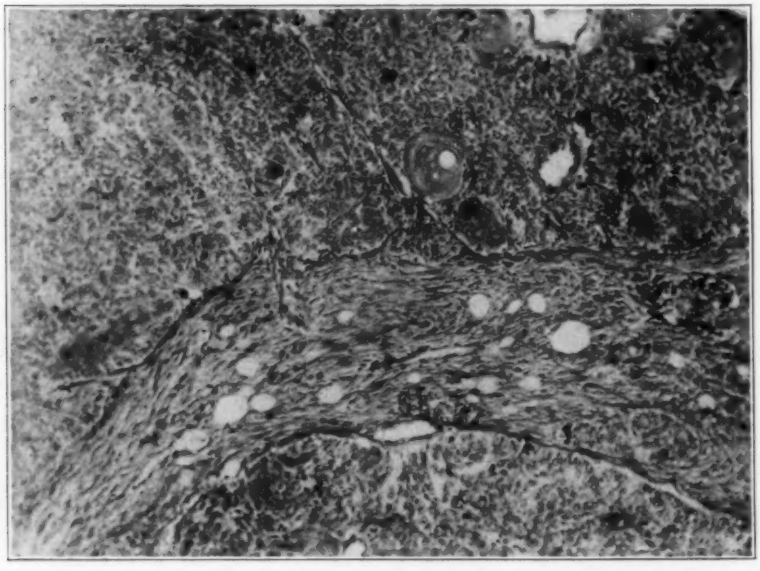

Fig. 20.—Low power magnification of tumor of heart muscle.

2. The collection of the fusiform cells into bands or whorls, resembling the appearance of gliomas forming after amputations.

3. The fibrillation of the protoplasm of the fusiform cells and the equally fibrillary structures of the stellate cells, similar to those seen in the gliomas of the brain (Lhermitte and Leroux).

4. The structure of the vessels, the walls thickened by the fibro-hyaline substance, the vascular obliterations.

We can conclude with Lhermitte and Leroux as to their ectodermic neuroglial, syncytial origin and can consider them as peripheral gliomas developing at the expense of the sheath of Schwann.

Conclusions: In Recklinghausen's disease the tumors are not of the connective tissue type of mesodermic origin. The tumors are all of the neuroglial type and are gliomas developing at the expense of the sheath of Schwann and hence are of ectodermic origin.

Stout [8] reported a case which presented certain points in common with my case. In discussing the case, Stout wrote:

Turning now to tumors arising in the peripheral nerves one is impressed with the fact that the literature is very scanty, but the majority of authors consulted seem to agree that whether single or multiple, malignant or benign, they are of mesodermal origin, coming from the epineural or perineural tissue. In 1906, on the other hand, Verocay described a case with multiple tumors of the nervous system which showed in many of the nodules in the peripheral nerves what he believed to be a marked growth of cells of the sheath of Schwann. He is thus the first author to suggest that the neurilemma cells may be the source of tumors of the peripheral nerves. This view is looked upon with favor by Borst writing in Aschoff's Text Book.

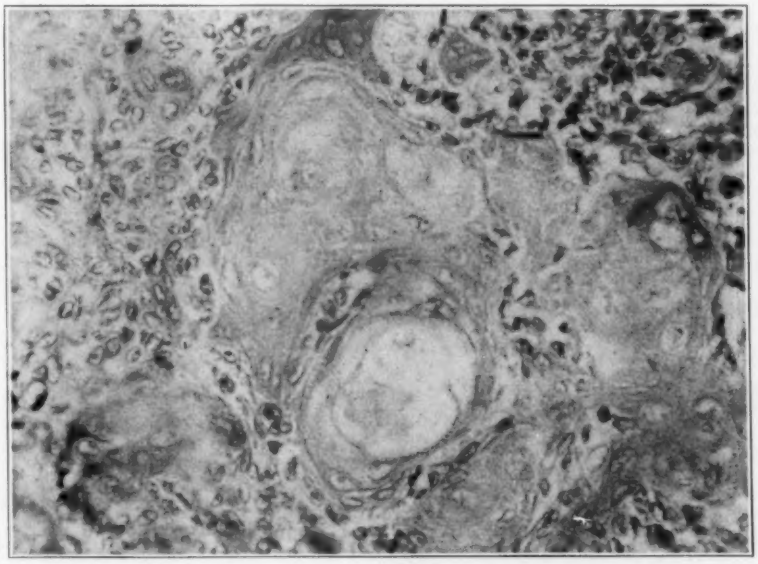

Fig. 21.—High power magnification of tumor of heart muscle.

In conclusion, it may be said that the tumor under consideration is a malignant neoplasm. Since the neurilemma of the peripheral cells is probably homologous to the neuroglia of the central nervous system it is suggested that this tumor may be a neoplasm arising from neurilemma cells or lemmocytes.

Lanford, in a previous report of this case, made the following observations:

Adami quotes Verocay to prove that the cells of the sheath of Schwann are of neuroblastic origin and that any tumor arising from the sheath is a neuroma. If this is true, we would be forced to include many of the tumors encountered in von Recklinghausen's disease and could find an explanation of the origin of our

8. Stout, A. P.: A Tumor of the Ulnar Nerve, Med. & Surg. Rep. Presbyterian Hosp., New York, 1918, vol. 10.

neoplasm, but our neoplasm did not show the characteristics of a neurogenic sarcoma until two previous growths had been removed.

The arrangement is very suggestive of epithelial origin, especially as the most actively growing cells are in glandular form.

The histology suggests very closely the histology of certain ependymal neoplasms. It is therefore necessary to resort to the theory that this neoplasm sprang from a cell which was carried down from the central nervous system in the development of the median nerve, it having its primary origin in the neuroepiderm of the developing embryo.

Percival Bailey [9] has described the typical ependynoma as follows:

The tumor is composed of a mosaic of polygonal cells with well defined cell borders and heavy, coarsely granular cytoplasm. The cells are crowded against

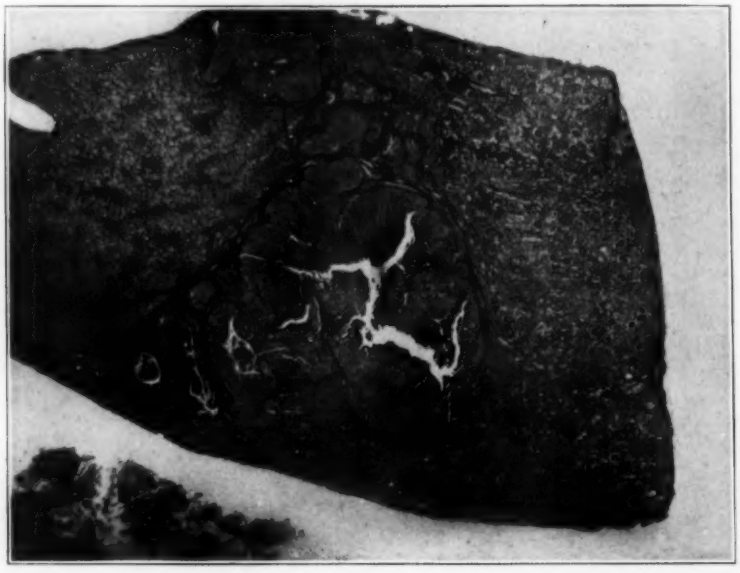

Fig. 22.—Low power magnification of tumor of kidney.

each other and have a single, large, vesicular nucleus. Among them may be seen a few coarse fibrils which stain poorly with methods for the demonstration of neuroglia fibrils. In certain areas the fibrils may be seen to be the continuation of one extremity of the cells. In these areas the cells are apt to have a tendency to arrange themselves radially around blood vessels or around channels whose walls contain a little poorly developed, often hyalinized connective tissue. No other connective tissue is present. In practically all the cells (probably all of the entire cells were included in the section) is to be seen a clear area containing sometimes one, usually two or three, rarely as many as a dozen small, clean-cut markings which stain heavily or by methods for demonstrating neuroglia fibrils, and may be spherical or short bacillus-like rods. These markings we have interpreted as blepharaplasten, or typical of ependymal cells.

9. Bailey, Percival: A Study of Tumors Arising from Ependymal Cells, Arch. Neurol. & Psychiat. **11**:1 (Jan.) 1924.

I can do no more than to leave this interesting tumor for further study by pathologists (Dr. Lanford and others) that it may eventually be properly catalogued.

Summary.—1. Recent investigations in embryology, particularly the work of Harrison, indicate that the sheath of Schwann is ectodermal in origin.

2. The clinical experience of Verocay and others indicate that neoplasms of the peripheral nerve arise from the cells of the sheath of Schwann.

3. These tumors of the peripheral nerve may be a part of systemic disease.

4. Recklinghausen's disease is not mesodermal in origin.

5. Penfield's work would indicate that he is in accord with these statements.

6. Epithelial neoplasms of peripheral nerves, when part of a systemic disease, may recur in the remains of the nerve, but they do not cause involvement of the lymphatics.

7. If recurrence occurs, amputation may be the only means of cure.

8. I believe that this tumor had its origin in the cells of the sheath of Schwann.

EPITHELIAL NEOPLASM OF THE RADIAL NERVE ASSOCIATED WITH NEOPLASMS OF LUNG, HEART, LIVER, BRAIN, DURA, CALVARIUM AND SUPRARENALS

CASE 2.—*History.*—Mr. J. J. G., aged 53, complained of symptoms which began in June, 1926, when he first noticed a hard lump in the "crease of the right elbow," which increased in size. On October 22, under local anesthesia a portion of the mass was removed by Dr. Metz. The mass recurred and became larger than before. He experienced pain, but function was not disturbed.

In March, 1926, he was told that he had tuberculosis, because of a cough and a purulent expectoration which was streaked with blood.

Examination—Examination was made on Dec. 13, 1926. There was a scar about 2¾ inches long on the lateral aspect of the right elbow. The skin on either side of this scar presented nothing of note. The right elbow was larger than the left elbow. There was apparently a diminished carrying angle and fulness in the antecubital fossa. The difference in size of the two forearms extended down to the wrist. The hand, on the palmar aspect, seemed slightly purple, in fact, the whole hand presented a mild cyanotic hue. When asked to pronate the forearm, he lifted the palm of the right hand up with the left; he called my attention to the fact that he was able to pronate the hand without the aid of the opposite hand, and demonstrated that fact.

There was tenderness and a noticeable difference in the size of all of the fingers, those of the right hand being slightly larger than the left. The muscles of the forearm were flaccid. The skin showed no difference in temperature. Palpation revealed all sensations present.

There was a mass which extended up to the middle of the scar and downward at least 1½ inches below the head of the radius. The mass seemed to be on the outer side of the biceps insertion. The skin moved freely over it. This mass was nodular, not painful and was movable in a lateral direction. Pressure on the mass did not produce any disturbance in the peripheral distribution of any of the main branches of the brachial artery. Apparently this mass did not have any deep attachment. Just above the external condyle and to the outer side of the triceps, there was a small nodular, firm mass which was not movable. The skin glided freely over the mass. I could not feel any axillary mass.

The patient was advised to have a roentgenogram of the chest made at once with the view of determining the operability.

He did not return until Dec. 31, 1926. At that time the following examination was made: On the outer side of the left elbow just lateral to the scar, the skin

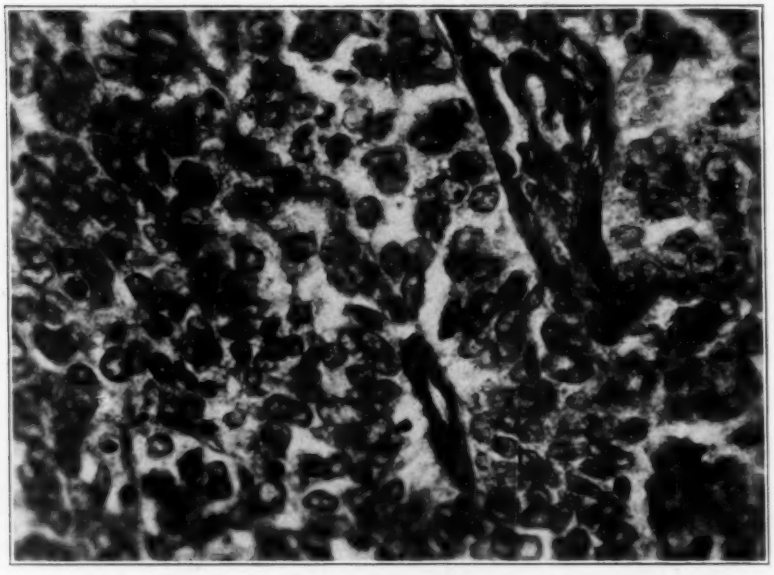

Fig. 23.—High power magnification of tumor in kidney.

had a bluish tinge. There was an irregular, nodular mass under this area. The level of the growth was four fingerbreadths below the external condyle and apparently under the supinator longus muscle. The upper limit of the mass was more than four fingerbreadths above the external condyle. The mass was movable in a lateral direction, but not up and down. The anteroposterior diameter of the mass above the elbow was about 2 inches. It was nodular, hard and painful. The mass extended upward along the upper border of the external condylar ridge of the humerus. There was limitation of extension of the arm, about 150 degrees, and flexion of 45 degrees. He was able to palmarflex and dorsiflex the wrist. Supination and pronation of the forearm were not impaired.

On the inner border of the biceps muscle, corresponding to about the middle of the arm in the course of the median nerve and brachial artery, there was a hard, nodular mass which was movable in a lateral direction, which was not movable up or down. It was not fluctuant. The size could not be diminished by pressure, proving that it was not a vascular dilatation, at least to my mind. Pres-

sure over this mass did not produce any disturbance in the peripheral distribution of the median nerve. Palpation in the axilla did not reveal any mass.

He was advised that "nothing short of a high amputation is going to be of any service."

Progress Notes.—Jan. 1, 1927: The patient was admitted to hospital for observation. The mass on the right arm, along the course of the radial nerve, was probably a malignant tumor of the nerve. He had a cough and raised bloody sputum. A roentgenogram of the chest was taken.

Fig. 24.—Liver showing metastatic tumor.

January 2: Roentgen-ray examination showed what was taken to be fluid in the right side of the chest with some pleural thickening.

January 3: An operation was performed. A diagnosis was made of recurring and metastazing epithelial neoplasm of musculospiral nerve; metastasis had occurred to the median nerve.

The radiologist reported that "there was no evidence of metastasis to the chest."

Operation: The arm was amputated. Wyeth pins were introduced in the front and the back and in the upper limit of the axilla, and a rubber tube tourniquet was used.

A circular type of incision was made. When the cuff of skin was retracted upward, the brachial artery was ligated. The axillary vessels were ligated. The median, ulnar and musculocutaneous nerves were cut high, and they were then "fish-tailed."

After this, the muscles were cut above, 1 inch higher than the skin cuff, the bone sectioned higher and the tourniquet released. Bleeding was not encountered. The muscles were quilted over, and the skin closed with interrupted dermol and fine continuous lock stitch.

The specimen was sent to the pathological department for inspection, section and dissection, and the following pathologic report was made: The axillary vessels lay on top of the median nerve and were closely adherent to the nerve. There was a groove on the inner aspect of this tumor mass made by the vessels. The median nerve could be dissected practically free from both vessels and the

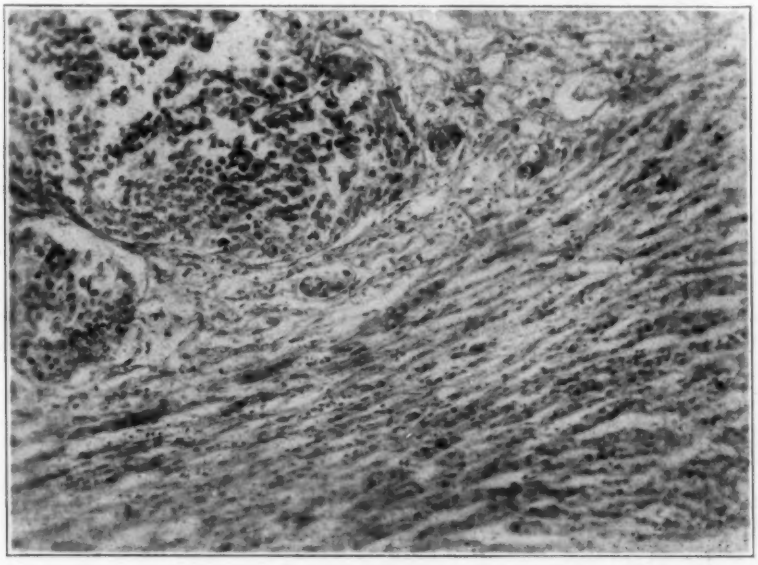

Fig. 25.—Suprarenal gland, low power magnification of tumor.

tumor. The tumor mass measured 3 by 1.5 by 1 cm. It was irregular and nodular. In places, it seemed to have broken through its capsule and was adherent to the surrounding tissue. On the outer side of the growth and overlying it was a large nerve trunk mass. Peripheral branches of the nerve were seen coming out of the lower nerve of the tumor mass. Along the vessel which accompanied the radial nerve small but similar masses were found. The wall of the vessel at this point seemed thicker as though it contained some new growth. There was a mass lying under the supinator longus muscle, which was about 6 by 3.5 by 2 cm. The upper portion of the muscle was normal in appearance, but the mass seemed to have invaded it. It was nodular and grayish. The radial nerve was dissected down and followed into the growth. Above the level of its penetration there was a small nodule; this mass seemed to be of the same character as the rest. The radial nerve below the muscle was dissected down to the wrist and was seen emerging from the mass, while the nerve itself was smaller than expected normally. The supinator longus was sectioned in its most prominent point and

the tumor mass exposed. The cut surface varied from pink to gray and was rather uniform, with the exception of a number of areas of small yellow comedones that exuded on slight pressure. The under portion of the cut sections showed rather distinct lobulations, especially where they had encroached on and distended the muscle. Blood vessels were not a prominent feature. There was an irregular and nodular mass, measuring 7 by 5 by 2.5 cm. which sprang upward on the lateral side of the triceps tendon. When cut, it presented exactly the same appearance as the outer tumor.

A section was taken from the neoplasm involving the supinator longus, triceps and in the bicepital groove epithelial neoplasm presenting islands of embryonal cells, the centers of which showed keratinization. The young cells were somewhat columnar, and a few groups showing a suggestion of glandular arrangement surrounding new growth was suggestive of glia tissue (Lanford).

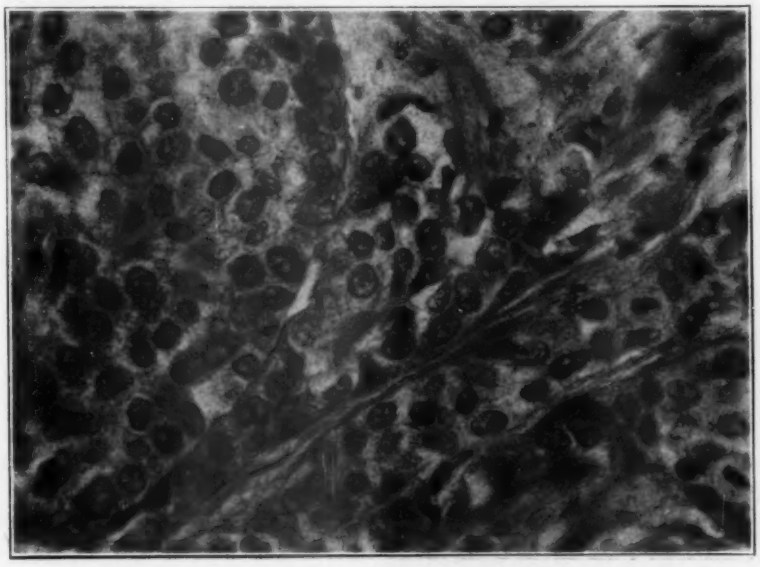

Fig. 26.—High power magnification of tumor of suprarenal gland.

On January 3, the roentgen-ray report stated that the left side of the diaphragm was smoothly contoured, the right obliterated. No increase in the size of the cardiac or great shadows was visible. In the upper reaches of the left side of the chest, small fan-shaped density was observed which was considered to be suggestive of an early tuberculous lesion. The same type of fluffy shadow was visible in the upper right side of the chest, and the changes were scarcely sufficient to warrant a positive diagnosis. In the base of the right lung, the diaphragm was obliterated, and a definite, fairly large density was observed of the type commonly seen when fluid obliterates the base. The pulmonary changes were insufficient to form the basis for a positive diagnosis of tuberculosis, although this must be considered as probable, but a neoplasm producing fluid cannot be ruled out. Consultation with the clinician was requested (Henderson).

On January 7, in the afternoon, the patient spat up a large amount of bright red blood and blood-stained sputum throughout the night. Hemoptysis occurred in the morning.

January 9: Hemoptysis occurred again in the afternoon. There apparently was an ounce of blood.

January 10: The dressing was changed in the morning. The patient still complained of some pain. A small amount of blood was present in the sputum throughout the day. The patient said that the lump in the top of his scalp was larger.

A consultation with Dr. Lemann, chief of the medical service, was asked. He reported "It is my impression that there is fluid in the pleural sac and I would recommend exploration with a syringe. In spite of suggestive history of preceding tuberculosis, I am inclined to believe we are dealing with a pulmonary metastasis."

January 11: A laboratory report showed that the sputum was examined twice; tubercle bacilli were not found, but gross blood appeared both times.

Fig. 27.—Tumor of spinal accessory nerve; low power magnification.

January 12: Profuse hemoptysis occurred in the morning. One-quarter grain (0.016 Gm.) of morphine was given twice, and 5 cc. of 10 per cent calcium chloride given intravenously.

January 13: The patient spat a little blood in the evening, for which morphine was given with good results; 5 cc. of calcium chloride was given intravenously.

January 14: The patient spat blood; 5 cc. of 10 per cent calcium chloride was given intravenously in the evening.

January 15: He did not spit blood. The dressings were changed and the sutures removed. The wound healed, with primary union. Five cubic centimeters of 10 per cent of calcium chloride was administered intravenously.

January 17: He had been spitting blood-streaked sputum the day before but morphine was not given. Five cubic centimeters of 10 per cent calcium chloride was given on that day and 5 cc. calcium chloride the following day.

January 18: The sputum was still streaked with blood.

January 19: The wound was dressed, and the patient allowed to go home, improved.

He returned on February 24 because of persistent headaches.

Examination showed a circumscribed, hard mass which was movable with the skin of the scalp.

On the right side of the abdomen on the outer border of the right rectus, there was a small circumscribed, hard, slight movable, painless mass about 1 inch (2.5 cm.) in diameter. This mass did not increase in size when the patient coughed, nor was it reducible into the abdomen. The patient was advised that it was impossible to tell the exact nature of the condition without operation. In view of the facts of his past history, I advised removal.

The wound on the stump was entirely healed. No mass was palpable in the stump. The skin over the axilla and the stump was freely movable. There was nothing to suggest a recurrence or metastasis of the axilla.

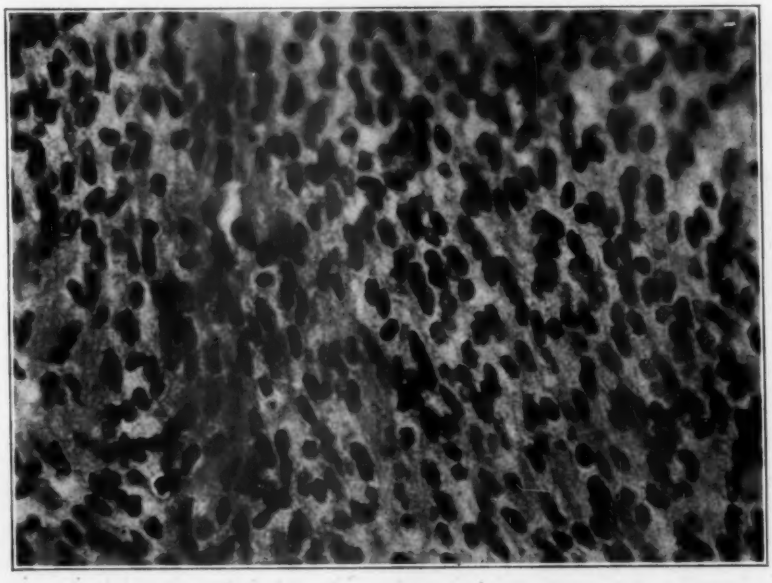

Fig. 28.—High power magnification of a tumor of the spinal accessory nerve.

Second Operation.—March 8, 1927: The preoperative diagnosis was tumor of the scalp and the abdomen. A diagnostic incision was made. In making preoperative diagnosis, the question arose as to whether we were dealing with metastasis from the original growth, or whether it was a cyst of the scalp.

An incision about 2 inches long was made over the most prominent portion of the tumor of the scalp. As soon as the skin had been reflected, we saw a solid tumor. We immediately realized that we were dealing with a malignant growth, and decided to remove a small portion for section. This was done and a specimen sent to the pathological department.

March 10: Since the operation, the patient had been restless and had complained that the weakness on the left side had been progressive. He lifted the left arm and forearm from the bed with difficulty. When the forearm was lifted up and the supporting force removed, the hand dropped. He had little grip. Loss of sensation in the distribution of the brachial plexus of the left side was noted.

There was some bulging of the right side of the chest and a flatness of the whole right side of the chest. Râles were not heard, and the respiratory sounds were clear. The voice sounds were transmitted, not distant, but, if anything, intensity was increased. At the base, the voice sounds were distant and there were no râles. The mass in the side had not increased in size. The patient continued to expectorate blood freely.

March 19: At 6 o'clock, the patient had a coarse tremor of the left arm, the left leg and the left side of the trunk. This coarse tremor was accompanied by a fibrillary tremor of the fingers of the left hand.

There was a decided deviation of the angle of the mouth to the right and also a widening of the left palpabral fissure. The weakness of the whole left side seemed to be becoming more prominent.

March 20 to 24: The patient was unable to raise his left arm. If the arm was elevated and the supporting force removed, the patient's arm dropped to the bed. There was a coarse convulsive movement of the left side (upper and lower extremities). The right pupil was dilated. Respiration was irregular, and the pulse became markedly irregular. There was progressive difficulty in swallowing as well as progressive stupor.

March 24: The patient died.

Autopsy Report.—Postmortem examination was made on March 25. The body was that of a white man measuring about 170 cm. in length and weighing about 140 pounds (63.5 Kg.). The head was covered with a full suit of black hair. The right arm had been amputated at the shoulder joint, and the scar was well healed. There was a scar on the abdominal wall about 1 inch from the midline extending along the costal border for 3 inches. There was an irregularity in the scalp corresponding to a firm irregular tumor mass that had extended entirely across the skull from one temporal ridge to the other; it involved about one half of the parietal bone anteriorly and extended backward to the occipital ridge.

When the peritoneal cavity was opened the gallbladder was found adherent to the wall; a number of adhesions were also found between the liver and the diaphragm; these were firm, but fairly easily broken up. The liver extended about two fingerbreadths below the costal border. There was no evidence of inflammation of the general peritoneal cavity. The appendix was retrocecal and showed a number of old adhesions. The cecum was found to be slightly distended, and the transverse colon was very much so. There was a small band of adhesions which were firmly contracted and empty. The lesser peritoneal cavity was normal. The lymph nodes were not enlarged.

When the sternum was removed, it was found to be adherent on the right side to the underlying structures of the right pleural cavity. The left pleural cavity was completely obliterated by firm adhesions between the wall and the lungs.

When the heart was removed, a cellular mass was found in the posterior portion of the sac. This was particularly striking between the entrance of the inferior vena cava and the superior vena cava. The mass involved the right lung and almost completely obliterated it.

The heart was flabby in consistency and dilated. The outer surface was pinkish red, and on the right ventricle there was a large soldier's patch. An irregular nodular secondary neoplasm was noted in the wall of the left auricle and a similar nodule in the wall of the right auricle. The endocardium was smooth, there being nothing within to correspond to the new growth on the epicardium. The attached portion of the aorta was the seat of a rather

early arteriosclerosis, small yellowish elevations being noted. The coronary vessels were markedly thickened, and in places, almost occluded.

The right lung was small and almost entirely obliterated by a new growth. The lower lobe was most involved. Attached to the lung and the bronchus, there was a large mass of lymph nodes which were almost entirely replaced by new growth. On section, the lobe was found to be practically destroyed and replaced by a cellular pinkish-gray structure containing a few areas of necrosis. The blood supply of the part was relatively scant. A small abscess cavity was found filled with pus. The upper lobe was the seat of many spots of new growth. The left lung was doughy and rather uniform throughout, no firm nodules being detected. In the apex, there was an area of tuberculosis, and posteriorly, an area of lobular pneumonia. A slight amount of fluid exuded on pressure.

The liver was slightly increased in size and relatively firm throughout. The dome on the right lobe, however, showed an area of increased consistency, but the outer surface over this area was smooth. In the lower portion of the left lobe, there was another area of increased consistency which had a rough and irregular outline and measured about 3.5 cm. in diameter. It was yellow. Throughout the entire anterior and superior surfaces of the liver were a number of tags of adhesions. On section, an enlarged tumor mass was found occupying the upper portion of the right lobe, measuring about 7 cm. in diameter. The tumor mass on section had a serrated irregular outline, and the cut surface was uniformly dirty yellow with a number of spots of necrosis.

The spleen was small and bound down by a few adhesions. It was flabby and slate gray, except a long irregular area of congestion across its anterior third. On sectioning, chronic splenitis was revealed, and some slight increase in the pulp was noted. Grossly, there was no secondary neoplasm.

The kidneys were slightly increased in size and rather flabby. They were more or less uniform throughout, except that in the left kidney there was a mass on its outer edge somewhat increased in density and oval in outline. On section, the entire cut surface was found rather uniform in appearance and presenting the picture of a toxic nephritis, and the area of increased density corresponding to a secondary growth. Several other areas of new growth were noted. The right kidney presented a similar picture but careful study failed to reveal any secondary neoplasm.

The right suprarenal was flabby, and an area of increased density was found, irregular in outline; on section this appeared to be a neoplasm. It was definitely within the border of the suprarenal and had destroyed it. The gross appearance of this new growth was the same as that of the new growth in the outer organs. The left suprarenal was normal.

The testicle was free from a new growth. The bladder was filled with cloudy urine. The prostate was normal, and no evidence of neoplasm, either primary or secondary, was noted. The retroperitoneal space was free from any new growth. When the scalp was removed the tumor was found firmly adherent to and infiltrating the aponeurosis of the occipital frontalis muscle; palpation showed that it had destroyed the bones. The dura was firmly attached to the brain in the parietal portion by a tumor mass which had entirely infiltrated it. The tumor mass on its upper portion was rough, irregular, pinkish gray and contained spicules of bone by means of which it was continuous with the calcarium. There were several depressions in the superior surface of the external parietal lobe of the brain as a result of the new growth pressing down. The under surface of the brain was normal. The pituitary gland was somewhat swollen, but otherwise normal. When the dura

was forcibly removed, it was found that the superior longitudinal sinus was free from involvement; the falx cerebri was also free of new growth. Sectioning of the brain showed the right cerebrum deeply infiltrated by the tumor mass for a distance of 1 inch in the middle portion of the parietal lobe and 1½ inches in the posterior portion; the new growth had extended over and pressed on the motor areas of the right side. The left side of the cerebrum was not infiltrated, the new growth being confined to the pia-arachnoid. The ventricles were normal.

The anatomic diagnosis was: carcinoma of the lungs and mediastinum; secondary carcinoma of the skull involving the dura; secondary carcinoma of the brain; secondary carcinoma of the kidney; secondary carcinoma of the liver; secondary carcinoma of the suprarenal; secondary carcinoma of the heart and pericardium; lobular pneumonia; chronic pleuritis; chronic splenitis; healed tuberculosis, pulmonary; toxic nephritis; dilatation of the heart, and acute splenitis.

The microscopic diagnosis was: squamous cell type carcinoma in the dura; brain, squamous cell type; in the suprarenal, secondary carcinoma with marked albuminous degeneration in the cortex; pancreas, normal; kidney, cloudy swelling, albuminous deposits and degeneration and chronic interstitial nephritis; spleen, chronic splenitis, passive congestion and amyloid deposits.

Summary.—1. This patient had a cough, hemoptysis and profuse purulent expectoration.

2. He had been treated for several months for tuberculosis.

3. He presented himself for examination after a tumor of the radial nerve had been excised.

4. The recurrent tumor at the original site was larger than the primary growth.

5. Roentgen-ray reports indicated fluid in the chest, without evidence of metastasis to the chest.

6. An amputation was performed.

7. A tumor of the scalp was later found to be malignant.

8. Prior to death, the patient developed progressive weakness of the left side of the body.

9. Autopsy revealed a carcinoma of the right lung, carcinoma of the skull, dura, brain, kidney, liver, suprarenal, heart and pericardium.

"All tumors resembled epithelioma, all, except the nerve tumor could be classified as carcinomata." (Lanford).

The difference between this and the first case is apparent.

Where was the original growth?

By searching the literature I found certain clues which may help to identify the present growth.

Is this a neurocytoma—neuroblastoma beginning in the suprarenals, or is it a metastatic carcinoma with the lung as the site of the primary tumor?

Like Marchand, it will have to be admitted at the outset that much that is hypothetical will have to be stated. If a mistake is made others will eventually correct our error.

In 1910, J. Homer Wright [10] called attention to a group of tumors the nature of which has hitherto escaped general recognition. The essential cells of the tumor are considered to be more or less undifferentiated nerve cells or neurocytes or neuroblasts, and hence the names neurocytoma and neuroblastoma. They are considered to be neurocytes or neuroblasts for the following reasons:

1. The cells, at least in places, are associated with delicate fibrils, often of considerable length, which do not stain like neuroglia, collagen or fibroglia fibrils by Mallory's methods, and which are like the fibrils occurring in the "anlage" of the sympathetic nervous system.

2. The cells associated with these fibrils have the same morphology as the cells from which the sympathetic nervous system and the medulla of the adrenal develop, and which are regarded by embryologists as arising from migrated primitive nerve cells.

The fibrils may be arranged parallel to one another in bundles which are intimately associated with masses of the cells, as are the fibrils with the neurocytes in the "anlage" of the adrenal of a human fetus in the fourth or fifth month.

The tumors reported were found in the liver, lungs, adrenals, calvarium, brain and retroperitoneal tissue.

The occurrence of these tumors in such a variety of situations is accounted for not only by metastasis but also by the generally accepted teaching that undifferentiated nerve cells migrate from the embryonic central nervous system to form the nerves and ganglia as well as the sympathetic system.

Moreover, it seems reasonable to believe that certain other small cell tumors without the characteristic fibrils, occurring in various situations, are also of this nature.

Lederer [11] reported a case in 1926, which he classified as a neuroblastoma of the suprarenal gland. R. S., a girl, aged 4½ years, two months before admission had a swelling which appeared on the left side of the head and the left eye became prominent. At autopsy, a tumor involving the left suprarenal was found.

The cranial bones were involved. Tumors in this region "were of an osteoclastic nature as evidenced by a cellular invasion and osseous absorption."

In discussing the case he said:

In the primary tumor the ganglion cells were in parts of the tumor, being present in groups, or scattered singly among the spindle cells. In the metastases, however, after careful and prolonged search, no ganglion cells could be discovered. This corresponds to the observations of most authors that these tumors metastasize only by virtue of the undifferentiated cells. The absence of differentiated cells in the metastases is the chief reason for both

10. Wright, Homer, J.: Neurocytoma or Neuroblastoma: A Kind of Tumor Not Generally Recognized, J. Exper. Med. July, 1910, vol. 12.

11. Lederer, Max: Neuroblastoma of the Adrenal Gland (Hutchinson Type): Report of a Case, J. Cancer Research, 1926, vol. 10.

clinical and pathologic error in diagnosis, since the picture usually resembles some form of sarcoma and the tumor is as a rule diagnosed as such.

As Reisman points out, the failure to recognize the condition clinically may be due to the small size of the primary tumor, rendering it impalpable.

Meltzer [12] reported two cases:

CASE 1. *Clinical History.*—The patient, a man forty years of age complaining of severe stabbing pain in the left chest, shortness of breath, and cough. Roentgen-ray pictures showed opacity of the left lower chest to the level of the fourth rib anteriorly. A diagnosis of pleurisy with effusion was made.

Autopsy: The left lung was densely adherent to the chest wall, and when torn away no pus sac was discovered, but a great deal of degenerated, odorless material. This material came from the necrotic lower lobe, the greater part of which was occupied by a large tumor mass of a grayish color, with red and yellow patches of softening. This tumor measured 7 by 7 cm. in its greatest diameter. At the upper pole of the right kidney, just slightly invading the kidney substance was a rounded, firm, yellowish white mass, measuring 3.8 by 4 cm. Small portions of adrenal cortex were seen adhering to the tumor.

A soft hemorrhagic tumor, measuring 6 by 3½ cm. was discovered in the right frontal lobe.

Microscopic examination: The adrenal tumor consists essentially of diffuse deeply staining cells, interspersed here and there with bands of fine, pale, fibrils. The cells vary slightly in size, but the majority consists of a small dark rounded nucleus, with a very scanty cytoplasm in some, but in most no cytoplasm is evident. Other cells are pyramidal in shape with again practically no cytoplasm. Where the cells are crowded together densely the nuclei are elongated. Numerous mitoses are seen. A few very large cells, undergoing division, are present. The delicate fibrillar bands stain pink in eosin-hematoxylin sections. They do not possess the differential staining characteristic of neuroglia, fibroglia or collagen fibrils. The tumor is very vascular. Numerous thin-walled blood vessels are seen, and red blood cells lying free among the tumor cells. The "rosette" arrangement previously described is not observed.

In the lung tumor the same appearance is accurately reproduced.

CASE 2. *Clinical History.*—A man fifty-three years of age. Pain across upper abdomen, cough, and frequency of urination were complained of.

Autopsy: The body is that of a much wasted man with a very prominent abdomen. On opening the abdomen it is seen that practically the whole cavity is occupied by a hugely enlarged liver, which reaches to the right anterior superior spine. The liver weighs 11 pounds and is uniformly involved in a malignant process, being studded with tumor masses of varying size.

The right adrenal is of normal shape, but appears to be slightly enlarged. When cut into a small rounded tumor measuring 8 cm. in diameter is found to occupy the medulla. The cortex appears normal in the gross.

The lung is heavy and consolidated. The lower lobe is covered with a recent exudate. When the lung is opened a white mass 4 cm. in diameter and roughly spherical in shape is seen at the hilus. Several smaller white nodules are scattered throughout the lower lobe.

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12. Meltzer, Sara: Neuroblastoma Occurring in Adults, Canad. M. J. **16:** 647 (June) 1926.

Summary: Neuroblastoma is a tumor almost confined to infancy, and early childhood. Both of the cases recorded in this paper occurred in adults.

In the microscopic picture one feature common to both tumors is the absence of "rosettes." We know that in the development of the sympathetic system the cells are frequently found arranged in rosette form. In the fully developed adrenal medulla these do not occur. This raises the possibility of some relationship between the age of the patient, and the finding of "rosettes" in the microscopic structure.

As the tumor is derived from the primitive nerve cell or neuroblast it may occur in any situation where such cells are encountered. It is, however, confined almost entirely to the sympathetic nervous system, and occurs most frequently in the medulla of the adrenal which itself is derived from that system.

It was pointed out some years ago by Frew that the site of the metastases depends on whether they are derived from the right or left adrenal. Thus if the primary tumor occurs in the left adrenal metastases will appear most frequently in the bones, especially the calvarium, but also in the liver and other organs, thus giving the first clinical variety. If the tumor is derived from the right adrenal, secondaries occur in the upper surface of the liver, the lung, and more rarely in the calvarium, and these fall into the second clinical group. We see that secondary growths occur most frequently in the skull, liver, and lungs, but they also occur in any of the bones, the sternum, vertebrae, ribs, and long bones: in the opposite adrenal, in the kidneys and even in the skin.

Apart from its position there is nothing characteristic in the gross appearances of a neuroblastoma. Microscopic, however, it possesses certain definite characteristics and a typical case can be recognized without difficulty.

Flemming and Davidson [13] reported a case in a boy, aged 4 years. The autopsy observations were:

The whole of the subcutaneous tissue of the scalp was replaced by a red fleshy mass of tumor growth. This growth covered the whole of the frontal, parietal, occipital, sphenoidal and part of each temporal bone on either side. It was dark red in color and had the appearance and consistency of muscle. Over the parietal bone the neoplastic mass was 1.5 cm. in thickness.

On section of the skull, the neoplastic growth was seen to penetrate the bone, so that most of the extradural space was occupied by a mass of malignant growth. There was very marked invasion of the internal surface of the frontal bone.

Suprarenal Glands. The left suprarenal was replaced by a large homogeneous, dark red, comparatively soft mass, 6 by 5.5 cm. in size.

Long Bones. Both those of the upper and lower limbs were definitely involved. The marrow was almost entirely replaced by tumor growth which invaded the bone, making it extremely friable and thin.

Microscopic Appearances—Primary Neoplasm. The tumor was composed of small cells which were either roundish or elongated in shape. There was very little cytoplasm present, the most of the cell being occupied by a nucleus which in many cases was hyperchromatic. In certain areas these cells tended to assume a "rosette" or circular formation. Interspersed among the cells was a meshwork of fine fibrils which did not stain with the specific stain for glial

13. Flemming, Robert A., and Davidson, James: A Case of Neuroblastoma (Neurocytoma), Tr. Medico-Chir. Soc., Edinburgh, 1924-1925, pp. 142-151.

fibrils or fibrous tissue. Comparing these neoplastic cells with the normal small round mono-nucleated cell, they were larger and more irregular in size and shape. The neoplasm was extremely vascular.

He summarized his observations and his study of the literature as follows:

As regards the occurrence of these tumors in such varied positions, this can be explained by the fact that the primitive nerve cells wander out from the embryonic central nervous system to form the sympathetic nervous system, and consequently tumors of this type may be found almost anywhere.

Finally, neuroblastoma may not be as rare as they were originally considered to be, as many which were or are diagnosed as sarcomata are really of nervous tissue. Of the two types neuroblastoma and ganglio-neuroma, the latter is the rarer of the two.

Of late years the interpretation of tumors of the nervous system has undergone many changes. For example, some years ago, the present case would have been classified as a sarcoma of the small round-cell type, but now it is recognized that neoplasms of the nervous system may be composed of the developing cells of the various parts of the nervous system. The neuroglia, or its various modifications may form tumors; as can also ganglion cells with nerve fibers, or the comparatively undifferentiated cell, which is the antecedent of these tissues. Thus we find tumors composed of cells which are the forbears of the sympathetic system, the chromaffin system, and the ganglion cells or neuroglial cells.

In the formation of the nervous system the epiblastic cells which line the medullary groove can develop into nervous elements or the supporting glial tissue. Nerve fibers may grow out from this central region and form the peripheral nervous system, or on the other hand neuro-epithelial cells may wander into the body and organs, and in relation to these organs give rise to the elements composing the sympathetic system.

In 1914, H. R. Wahl[14] reviewed the subject of neuroblastoma. He reported:

It is becoming recognized, especially in the last four or five years, that the most highly differentiated tissue of the body—the nerve tissue—may and does frequently undergo blastomatous change. True nerve tumors, i. e., growths consisting of specific nerve elements, may occur in any part of the nervous structure, but by far the greater number of them have their origin in the sympathetic system. These tumors may be either benign or malignant.

In his summary and conclusion, he stated:

Nerve tissue may give rise to new growths, which are properly called neuroblastoma.

Neuroblastomata are manifestations of a pathologic condition more or less localized or diffused in the whole or part of the nervous system. If localized to one focus, as is usually the case, the result is a solitary nerve tumor (ganglioneuroma); if generalized, multiple tumors result.

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14. Wahl, H. R.: Neuroblastoma, with a Study of a Case Illustrating the Three Types That Arise from the Sympathetic System, J. M. Research, 1914, June, vol. 30.

Owing to the extensive variation in the degree of differentiation of the cellular and fibrillar structures in the undifferentiated type of nerve tumors different portions of a malignant neuroblastoma may differ widely in their appearance.

The possibility that this case represents metastatic carcinomas with the lung as the site of the primary growth cannot be overlooked.

Reference to Barron's excellent work on carcinoma of the lung is convincing. He stated:

The metastases from lung carcinomas are frequent and numerous. According to Adler, the principal metastases in his collection of 374 cases were to these organs: (1) lymph nodes, 117; (2) liver, 103; (3) lungs, 66; (4) kidneys, 58; (5) suprarenals, 38; (6) brain, 28 (dura mater, 10), and (7) bones (vertebrae, 5).

Briese, in his series of sixty cases, found metastases absent in only four cases. Of the twenty-one organs and tissues listed in the order of frequency, the principal ones involved were: (1) regional lymph nodes, 43; (2) liver, 25; (3) pleura, 17; (4) kidney, 17; (7) lungs, 11; (8) brain, 11; (9) bones, 9; (12) ovary, 7; (13) suprarenals, 6 and (17) dura, 3.

It is true that none of his collected cases present evidence of metastases to peripheral nerves, but there is evidence of metasases to the brain and spinal cord.

The other organs involved in our case are frequently involved in cases cited (liver and suprarenals).

Brunn stated:[15]

Metastases occurred in 85 per cent of the cases. Many of the initial symptoms were due to metastatic involvement. These occur relatively early and may be the condition that brings the patient to the doctor. A great many of the clinical diagnoses were made on metastatic involvement, mainly cerebral or bone involvement. The brain was involved in 12 per cent of the cases, the liver in 30 per cent, and the kidneys in 20 per cent. Two striking features in the occurrence of metastases are that the heart was involved in 21 per cent of the cases and the suprarenals in 14 per cent in a study of 626 case reports.

Lanford stated specificially that all of the growths may be considered metastatic carcinoma, except those of the nerve.

We know this patient had evidence of lung involvement before the tumor of the nerve appeared. Reference to his history shows that he was treated for tuberculosis long before he came under our observation. This is a common error.

Summary.—My second case illustrates a type of malignant epithelial neoplasm which not only recurs in the original nerve, but which may involve other peripheral nerves.

15. Brunn, Harold: Primary Carcinoma of the Lung, Arch. Surg. **12**:406 (Jan.) 1926.

Whether this is a neurocytoma or neuroblastoma of the variety described by J. Homer Wright or whether it is a metastatic carcinoma with the lung as the site of the primary lesion, cannot be definitely stated at this time.

Neoplasms of the peripheral nerves associated with evidence of pulmonary lesions should certainly direct attention to the lung as a factor before operative intervention is resorted to.

The recognition that true tumors of the nerve, either benign or malignant, do occur in any part of the nervous system should be more generally appreciated.

ENCAPSULATED TUMOR OF THE SPINAL ACCESSORY NERVE

Solitary neoplasms of cranial nerves must be considered when differentiating masses in the neck. This single point is my reason for adding the third case to this presentation.

CASE 3.—Mrs. G. L., aged 53, was referred by Dr. I. I. Lemann because of the presence of a swelling on the right side of her neck. This swelling had been noticed only two months before she came under observation. There was a history that the mass increased and diminished in size. She complained that the mouth was dry and that recently there had been a small amount of saliva. Pain was not associated with the mass.

This patient had been under Dr. Lemann's care because of hypertension.

Tonsillectomy had been performed by Dr. R. C. Lynch one and one-half years before the present examination. Following the operation, there was a secondary hemorrhage which was controlled by sutures.

Examination.—She was examined on April 29, 1927. There was swelling on the right side of the neck which extended down to the upper level of the thyroid cartilage. The mass lifted up the sternomastoid muscle and seemed to extend upward to the tip of the mastoid. The skin over it was neither red nor glossy. Pulsation was not noted in the mass. There was a pulsation below the level of the mass, and this pulsation seemed to extend upward from the junction of the middle of the upper third of the clavicle and reached the sternomastoid about its middle posteriorly. A pulsation was noted in front of the mass, and this corresponded to the facial artery.

No palpable mass was found about the ascending ramus of the mandible on the right side. When the patient opened and closed her mouth, the condyle immediately under the skin could be palpated. The glands in the digastric triangle on both sides were palpable. There was a mass, the lower limit of which corresponded to the upper limit of the thyroid cartilage, which could be palpated as high, I believe, as the tip of the mastoid. The mass was not adherent to the muscles and could be moved laterally. It was not nodular, but seemed to be smooth. No pulsation was imparted to the finger. I could get a lateral range of motion of about 1 inch. The floor of the mouth did not show bulging, and with the finger in the mouth I could feel a mass lying immediately on top of what I believed to be the internal carotid artery. The mass did not cause any bulging of the posterior pharyngeal wall. There was no bruit over the mass.

The diagnosis was probable tumor of the carotid body.

From my examination, I had the impression that it was a tumor of the carotid body for the following reasons:

There was a discrete, smooth, nonpulsating mass which had lateral mobility, but none in the long axis of the body. It was not adherent to the underlying structures. There was nothing which in any way would lead one to suspect aneurysm because of the absence of expansile pulsation and also because of the absence of bruit.

Primary carcinoma of the lymph glands of the neck is so rare as to rule it out ordinarily; more than that, the lack of fixation, the fact that the mass was discrete and that there were no similar masses seemed to eliminate carcinoma.

The blood dyscrasia seemed to be ruled out by the observations of Dr. Lemann. Cysts in the neck, branchial, thyroglossal, ranula were not usually found at this age. Aberrant thyroid must be considered, but the smooth, rounded contour seemed to eliminate that in my mind. Syphilis and tuberculosis seemed to rule themselves out on many grounds.

The diagnosis of tumor of the carotid body was made both by elimination and by the manifestations present.

The operation was not performed until July 13, 1927.

The preoperative diagnosis was undetermined, but several conditions were considered among which were a tumor of the carotid body, branchiogenitic carcinoma, aberrant thyroid and possibly a cured false aneurysm.

An incision was made from the tip of the mastoid process, 3 inches in length, extending along the anterior border of the sternomastoid. The sternomastoid was reflected outward and the carotid vessels and jugular were exposed and retracted medially. The sternomastoid was lifted up, and the tumor could be palpated under it as far as the angle of the jaw.

The parotid gland was exposed at the upper angle of the incision. In order to have better exposure of the tumor, a second incision was made, beginning at the upper limit of the original and extending obliquely downward and backward along the mastoid process for about 2 inches.

The sternomastoid was cut across and reflected. This permitted us to obtain a free exposure of the mass. A tumor mass, about 1½ inches long and ¾ of an inch wide was seen to occupy a position immediately lateral to the great vessels of the neck. The upper limit of the mass was continuous with a small "cord," the lower limit was continuous with a similar "cord" which extended down a short distance paralleling the vessels. The tumor itself, between the upper and lower structure, with which it fused gave the appearance of a punching bag suspended from a ceiling and held fast by an attached cord to the floor. The fibers of the cord above and below spread out over the bulbous enlargement like a fan. The upper portion of the cord could be followed upward under the mandible.

When an attempt was made to dissect the tumor away from this fanlike projection over its surface, we found that this was impossible.

The tumor was excised well above the upper limit of the bulbous enlargement and well below the bulbous enlargement. While we were removing the mass, that portion which had previously been described as being thin-walled ruptured, and a dark-yellowish material (which did not give the impression that it was gaseous) was spilled in the field. The mass was removed and turned over to the pathologist. All bleeding points were clamped and ligated, muscle planes approximated and skin closed. A gross section of the tissue showed a cavity with smooth, thick walls and many blood vessels

running across it, giving the appearance of a myxomatous tumor. The cord previously mentioned looked like a nerve bundle.

Progress Notes.—Convalescence was uneventful except for slight parotitis. The wound healed primarily.

The laboratory examination (July 13) showed the specimen to be an irregular oval mass of tissue, measuring about 5 cm. in diameter, with a small projection about 0.5 cm. thick and apparently made up of a number of individual fibrils suggesting a nerve. The outer surface varied in color from a red to a yellow tinge, and the entire mass was pseudo-encapsulated. It was soft, but uniform. On section, it offered little resistance to the knife and presented a cut surface that varied from a light pearly gray to a pinkish tinge and was divided into irregular lobules by a connective tissue of increased consistency. The blood vessels were not prominent. Cellular neoplasm of undetermined type was diagnosed.

Microscopic examination showed that the specimen was made up of a number of cells occurring in irregular masses which were differentiating into nerve tissue. Some of the cells showed large vesicular nuclei, and in others, mitotic figures were present. The older cells showed a relatively well defined nuclei and a cytoplasm scanty for the most part and divided into innumerable little fibrils which were anastomosing with similar fibrils from other cells. The histology suggested glioma, whereas other areas suggested a more cellular form of neoplasm.

The diagnosis was neurocytoma (Lanford).

August 8: The examination following operation showed that the wound was entirely healed. There was no discharge. There was still some enlargement of the right side of the neck, and the skin was infiltrated. There were enlarged glands in the supraclavicular region. There was atrophy of the trapezius, supraspinous and infraspinous muscles of the right side.

The patient did not voluntarily completely extend the right elbow. The right shoulder was lower than the left. She volunteered the statement that she was unable to get her arm up to comb her hair.

August 10: She returned to the hospital, where 1,950 mg. hours of radium treatment was applied to the right side of the neck.

August 27: Atrophy of the muscles about the right shoulder was noted.

November 21: The right shoulder was much lower than the left. The clavicle was prominent, particularly near the acromioclavicular joint. There was a definite depression on either side of the clavicle at the outer end. Marked atrophy of the trapezius and supraspinous and infraspinous muscles was noted. Abduction of the arm was painful, and atrophy was more prominent when the arm was abducted.

Voluntary extension of the elbow was limited to about 150 degrees. Passive extension beyond that point was painful.

There was no limitation of rotation of the head. When the head was inclined to the left side, there was some discomfort as of stretching. No mass was palpable in the mouth.

The operative scar was smooth and freely movable. There was no palpable mass in the region of the previous tumor.

This tumor was solitary, encapsulated and developed along the course of one of the cranial nerves. For these reasons, it seemed to fall in the same class as neurinoma and acoustic neuroma. This classification is correct if the tumor arose from the sheath of Schwann, according to Verocay and Cushing. Lanford's description would seem to place it in this category.

Penfield [16] denies that this group arises from this source. He stated:

> The fibers produced in these neoplasms show that the type cell bears no relation to neuroglia nor to the ectodermal sheath of Schwann cells.
>
> Mallory (1920) in a careful histological study of the type cell of the so-called dural endothelioma suggested that the fibroblast was the type cell of the nerve sheath tumor as well as of the "endothelioma." He therefore proposed the name "peri-neurial fibroblastoma," assuming an origin from the connective tissue which surrounds the nerve. Inasmuch as we have found that the fibers in these tumors are not neuroglial and not nervous in nature but represent a particular form of collagen it is obvious that we must confirm Mallory's opinion provided the neurofibromata be excluded from the group.
>
> The perineurial fibroblastoma must be considered to arise from the perineurial or endoneurial connective tissues which invests nerve fasciculi and fibers.

CONCLUSIONS

1. It may be presumptuous to attempt to classify this tumor in accordance with Verocay, Cushing and Lanford, in opposition to Mallory and Penfield; yet in view of the fact that I believe that the sheath of Schwann is ectodermal in origin and the fact that Lanford found cells which suggest "differentiation into nerve tissue," I believe that it is justifiable to consider this an epithelial neoplasm.

Future investigation may change the designation.

The essential points for us as surgeons are:

2. To recognize that solitary tumors of the nerve occurring in or on a peripheral or cranial nerve occur more frequently than we have accustomed ourselves to believe.

3. These tumors must be considered when masses in the neck are differentiated.

4. This tumor of the spinal accessory nerve was solitary. Up to the present time, the patient is comfortable, without any evidence of further trouble.

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A REVIEW OF UROLOGIC SURGERY

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KIDNEY

Surgical Technic.—Rovsing [1] discusses his technic in operations on the kidney. The conditions most conducive to good results are the position of the patient and the incision which will give free access to the swollen, friable and adherent kidney. According to his procedure, the patient is placed on his back, in such a position that the edge of the table coincides with the free border of the erector spinae muscle, from which the lumbar region is readily accessible for the incision that begins midway between the twelfth rib and the iliac crest and continues forward to the border of the rectus muscle in cases of large tumor. In cases in which the ureter is to be exposed, the incision passes around the anterior superior spine of the ilium obliquely down toward the symphysis pubis. Through this incision, the hand may be introduced into the retroperitoneal space, and the kidney carefully and definitely isolated from its surroundings, thus bringing it uninjured outside the wound. This is important in ordinary suppurative processes, and in cases of tuberculosis and malignant tumors it is absolutely necessary in order to insure a good result.

In case a single stone lies free in an aseptic renal pelvis, Rovsing does not remove it through an incision in the pelvis. As a rule, he performs nephrolithotomy in the following manner: The stone is held between the thumb and index finger of the left hand, while an incision is made with a small knife in the capsule on the convex side of the kidney over the site of the stone. A forceps is then forced through the renal tissue on to the stone, dilating the opening so that a stone forceps may be inserted and the stone removed. This method does not

1. Rovsing, N. T.: My Technic in Operations on Kidney, Practitioner **118:** 164, 1927.

cause the injury that knife incision of the parenchyma would cause. Hemorrhage is avoided both during and after operation. Collective statistics on nephrolithotomy indicate that hemorrhage is usually frequent. At the International Urological Congress in Rome in 1924, collective statistics were given in 686 cases of nephrotomy; serious bleeding occurred in 85 (13.5 per cent) and 22 of the patients died.

If nephrectomy is indicated in cases of malignant tumor, tuberculosis or pyonephrosis, Rovsing begins by doubly tying the ureter with silk a few centimeters below the pelvis, and with cautery sears through the ureter slowly and cauterizes the mucous membrane in the lumen. Next, the kidney is isolated, care being taken that the capsule is not ruptured. The vessels are ligated with strong catgut and the kidney delivered through the wound. Then an incision 2 cm. long is made through the skin and fascia in the iliac fossa. A blunt perforation in the muscles and peritoneum is made and the peripheral stump of the ureter is drawn through and fixed to the skin. This guards against infection from the ureter, and in tuberculosis any subsequent tubercle of the ureter and bladder can be treated by the injection of a solution of carbolic acid.

Rovsing regards nephrectomy in polycystic kidney as inexcusable, even though some patients survive the operation. The disease is always bilateral and so little functioning renal tissue remains that uremia is not infrequently a sequel to the removal of one of the kidneys. It is essential to protect and set free as much as possible of the remaining kidney which is compressed by the tension of the cysts. This is done by multiple puncture of the exposed kidney which reduces it to normal size. The kidney is replaced and the wound closed around a drain. Oozing of urine or a chronic urinary fistula never occurs. Relapses are rare and renal function improves immediately after this type of conservative surgical procedure.

Rovsing uses a simple method of nephropexy which has the advantage over other methods of fixing the kidney securely in an absolutely normal anatomic position without injury, without leaving foreign bodies and without fixing the kidney to osseous structures. An angular incision is made, starting externally to the erector spinae muscle at the level of the tenth rib, passing perpendicularly down to midway between the twelfth rib and the iliac crest, and from there going forward for 10 cm. The kidney is drawn out through this incision, after being carefully loosened from its adhesions to the peritoneum and fat capsule. Retracted strands of fascia along the ureter are severed or loosened with a blunt instrument, as they tend to draw the kidney down again and cause pain. The membrane is incised longitudinally from the upper end to the juncture between the third and fourth quarters of the kidney, and from the ends of this incision, transverse ones are made out to the

sides. The membrane is then separated with the help of a flat sound, so that it looks like two folding doors or wings out to the sides. A strong piece of catgut is passed in and out through the portion of the membrane attached to the lower end of the kidney with a special needle curved on the flat plane. The ends of the catgut suture are next threaded through large curved needles and passed out through muscles and fascia to each side of the upper end of the lumbar incision. They are tightened until the kidney in the loop of catgut is drawn up into the exact normal position, and are tied over the fascia at the level of the tenth rib. The lumbar wound is sutured in four stages, the fascia and the skin with metal, and the muscle with catgut. After a period of from ten to fourteen days, the kidney is fixed in the normal position by the two wings of membrane. Rovsing has performed this operation about 300 times and considers it almost ideal. Pain entirely disappears, and in only 10 per cent of his cases has it partially returned.

Rovsing first performed nephrolysis in 1892, in a case of medical nephritis of the type which is now called nephrosis. Since then he has performed operations in at least 100 cases of nephritis that had been refractory to medical treatment, with an operative mortality of 4 per cent.

In cases of painful horseshoe kidneys without infection or other complications which would necessitate removal of one kidney, but in which it is simply a question of preserving all the renal tissue, Rovsing performs laparotomy through an incision in the rectus muscle, and exposes the isthmus by an incision in the posterior sheet of the peritoneum. The tissue of the isthmus is slowly crushed through with a powerful angiotribe until only the capsule persists. The angiotribe is removed and replaced by two narrow clamping forceps between which the capsule is cut through. The capsule is sewed close to the renal tissue with a continuous catgut suture, the forceps are taken off, and the liberated kidneys immediately retract into their respective beds. The two peritoneal wounds are carefully sutured and the abdominal incision closed.

Surgical Complications.—Mathé [2] reviews 370 cases of disease of the kidney in which operation had been performed in St. Mary's Hospital, San Francisco. The most common complications were shock, hemorrhage, cardiac lesions, phlebitis and embolus.

Surgical shock or exhaustion occurred most frequently in cases in which a considerable amount of blood had been lost after the removal of a large kidney. All bleeding points should be securely ligated during the operation. Loss of blood should be particularly guarded against in

2. Mathé, C. P.: Renal Surgery: Its Pitfalls and Complications, California & West. Med. **28**:57, 1928.

children. Mathé employs the silver wire method in opening the parenchyma of the kidney, and during the procedure he clamps the pedicle in order to lessen hemorrhage. He uses a double layer of mattress sutures to close the kidney. Fat is included in these sutures to prevent postoperative hemorrhage.

Phlebitis occurred in 2.8 per cent of Mathé's cases. It usually occurred in the internal saphenous vein. Treatment consisted of rest, compresses of hot boric acid and elevation of the affected member. Quinine, given either by mouth or intravenously, seemed to hasten recovery.

In thirty-two cases of nephrectomy for tuberculosis, the wound healed in the average time of ten weeks, and in nephrectomy for pyonephrosis, the average was three weeks.

Mathé pays careful attention to cardiac complications; in most of his cases the heart is examined by a competent internist before operation. Some patients are put on a digitalis regimen prior to surgical intervention. Mathé gives 15 drops of a digitalis product hypodermically every four hours after the operation until the pulse reaches 70. Although the peritoneum was opened on a number of occasions, symptoms of peritonitis did not develop. Usually, operations on the kidney can be performed extraperitoneally. In dissecting out large adherent tumors care should be taken not to injure the pleura. In case the pleura is injured, low-grade pleurisy develops, which usually clears up in a week or two.

In 50 cases in which operation was performed between 1906 and 1916, a period before complete urologic examinations were made, the mortality rate was 6 per cent. Between 1916 and 1926, the mortality was 2.04 per cent in 320 cases. A careful estimation of the renal function and a study of the working power of the opposite kidney allows elimination of cases with a poor risk.

Hinman, in discussing Mathé's paper, did not feel so confident about the safety of leaving clamps in place following nephrectomy, as Mathé has done in a number of cases. Hinman calls attention to a rather high percentage of fatal postoperative hemorrhages following release of the clamps, and he expresses the opinion that the clamps should not be left on except in extreme emergency. He has not left clamps on during the last ten years. He always carries out hypodermoclysis during the operation, so as to supply plenty of fluids to the patient before he recovers from the anesthetic. Hinman believes that a large proportion of failures in conservative as well as radical operations on the kidney are due to secondary infections. These infections are produced or made more serious by rough and prolonged operation. Dispatch at the time of operation is one of the greatest assets of successful renal surgical procedures.

Manson states that he agrees with Hinman concerning the leaving of clamps on the renal pedicle. If the clamps are left on, they should be removed with the greatest care by loosening a notch or two at a time for one or two days before complete removal. Too rapid or rough removal of a clamp may open up a vessel and start bleeding. Manson believes that the perirenal fat is frequently involved with the tuberculous kidneys, and should usually be removed also. He does not remove the ureter, but sutures it to the skin at the lower angle of the wound; in this way the wound does not break down.

Renal Decapsulation.—Molina [3] reports several cases of mercuric poisoning. One case was that of a young woman who had absorbed 2 Gm. of mercuric chloride. Various forms of medical treatment did not prevent the appearance of anuria. Bilateral decapsulation of the kidneys was performed thirty-six hours after the onset of anuria. The patient gradually recovered and passed a normal amount of urine. She was completely cured nineteen days after surgical intervention.

In comparing the surgical with the medical results, Molina agrees with Pousson, Legueu and Tisserand, that in cases of toxic nephritis, it is absolutely necessary to perform an operation as soon as anuria sets in. The operation, which should be performed quickly and without shock to the patient, does not cause disturbance of the renal function later.

[Ed. Note.—Quinby [4] reports a similar case in which decapsulation was performed for acute tubular nephritis from mercuric chloride poisoning. This patient was not benefited by the operation, and died five days after the onset.]

Contusions.—Klenka [5] reports three cases of wounds of the kidney. The first case was one of traumatic rupture of the kidney. Cure followed suture of the renal tear. In the second case, the upper third of the kidney had been torn away. Hematuria did not set in until seven days later. In this case, it was necessary to perform nephrectomy. In the third case (rupture of the kidney), the patient refused operation, for two months hematuria was intermittent and accompanied by fever. Nephrotomy was finally performed and a large perinephritic hematoma was found. The kidney was markedly congested but an outstanding tear was not found. Klenka believes that numerous fine lesions were present, but invisible macroscopically. The pressure of the hematoma against the kidney probably stopped the bleeding.

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Nephropexy.—Petit,[6] who studied the late results in a series of cases in which nephropexy was performed during the last twelve years, concludes that this operation gives more lasting and better results in cases in which there is renal retention or persistent oliguria. The results are less satisfactory in cases in which nephropexy is performed because of pain in the region of the kidney without other urinary distress.

If patients are in pain because of a movable kidney, and are nervous and dyspeptic, signs of renal retention should always be investigated. This should be accomplished by means of ureteral catheterization.

If orthopedic or medical treatment does not relieve the patient, nephropexy should be performed because such kidneys usually contain fibrous or perinephritic lesions which diminish their functional value and predispose them to infection.

Foreign Bodies.—Brattstrom[7] reports a case in which two grass straws covered with concretions were found in the renal pelvis. The straws had probably been introduced through the urethra to the bladder and had found their way into the ureteral orifices and later the kidney. Nephrectomy was performed.

Tuberculosis.—Kidd[8] states that tuberculosis of the urogenital tract is a disease of adolescence, as common in males as in females, and induced by the stresses of puberty, work, marriage and parenthood. Clinical experience suggests that the human and bovine type of *Bacillus tuberculosis* produce two different types of disease. The first runs a rapid course and proves fatal in two or three years, a type which may be due to an infection with the human strain of the bacillus. The second runs a slow course of from ten to twenty years, in which the prognosis is excellent after surgical intervention, and in which the bovine type of bacillus may be concerned.

The bacillus is absorbed into the blood stream and may infect the kidney, seminal vesicle or testicle primarily, and no other organ of the body. In most cases, tuberculosis of the kidney appears as a unilateral blood borne infection. In women, the disease always starts in the substance of a kidney and extends into its pelvis, producing pyuria and increased frequency of urination. In men, the disease may start primarily in the testicle, extending along the lymphatics of the vas to the vesicle, prostate and base of the bladder, or it may start in both the testicle and the kidney.

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6. Petit: Les résultats lointains de la néphropexie, Presse méd. **2**:1365, 1927.

7. Brattstrom, Erik: Unusual Case of Foreign Body in Kidney, Acta chir. Scandinav. **62**:56, 1927.

8. Kidd, Frank: Treatment of Tuberculosis of Kidney, Practitioner **118**:150, 1927.

The most deceptive feature of tuberculosis of the kidney is the absence of pain in both kidneys until the later stages of the disease, and it is difficult to realize that one of the kidneys may be destroyed by the tuberculous process. The healthy kidney may ache at times because it is heavy, having increased to double its size in order to carry on the work of both kidneys.

In the more acute types, the onset of symptoms is an attack of profuse hematuria, which may be repeated once or twice. Pyuria is one of the most constant signs, but in chronic cases there are periods in which the pus disappears from the urine entirely, owing to ureteral obstruction. The general condition of the patient is usually satisfactory for the first year or two except in acute cases. There is no anemia or wasting, and there is no fever as long as the infection remains unmixed; later secondary infection from colon bacilli may occur which will induce fever.

In cases in which it is impossible to see the ureteral orifices, Kidd makes a small abdominal incision just below the umbilicus. Through this he inserts a gloved finger and palpates the ureters on each side as they cross the brim of the pelvis. If one ureter is thick and the other normal, and if the blood urea is within normal limits, he removes the kidney on the side of the thickened ureter.

Tuberculosis of the kidney inevitably leads to death after years of pain and misery unless the kidney is removed by operation. Early diagnosis, followed by nephrectomy, results in complete cure in at least 60 per cent of the patients so treated. In expert hands, due to the precision and accuracy of urologic diagnosis and surgical procedures, the mortality following operation should be less than 2 per cent. In 65 consecutive cases there were no deaths; the condition of 38 patients was observed until they were completely cured, in a number of instances from ten to fourteen years after operation. These data indicate that between 50 and 60 per cent of the patients should obtain permanent cure. Healing occurred by first intention in 36 of the 65 operations. Kidd removes not only the kidney, but the fatty capsule intact.

Legueu and Chevassu report 708 cases in which nephrectomy was performed for tuberculosis. Half of the patients were completely cured, one-fourth were improved, and one-fourth died within ten years after operation. They reviewed 638 cases in which the treatment was nonsurgical; 356 patients (51 per cent) died, mostly within from two to five years; 282 were alive, 22 more than ten years after the diagnosis had been made. They review data on 184 cases in which tuberculin was used; 51 of the patients were believed to have been cured.

Wildbolz performed an operation on 445 patients for renal tuberculosis; 11 (2.4 per cent) died within six weeks of heart lesions or embolism. Four hundred sixteen patients had been operated on before

1920, and details were obtained concerning 317. One hundred ninety-five of the patients (61.5 per cent) were cured; 28 (8.7 per cent) were not cured and 94 (29.9 per cent) died subsequent to the operation. One hundred and four of 125 patients operated on more than ten years previously were traced; 44 were dead; 58 (55.7 per cent) were cured and remained well.

Judd and Scholl report 863 nephrectomies: 611 patients were traced; 58 per cent were cured, and 31 per cent had died.

Wildbolz employs injections of tuberculin in many of his cases. The process of cure in these cases had been more certain and more rapid than in those in which tuberculin was not used. He believes that small doses of tuberculin are efficient. Small doses stimulate resistance, but large doses overwhelm and break down resistance. Kidd employs Koch's new tuberculin. Tuberculin should not be given until six weeks after an operation, and doses should be started with 0.00001 mg. If at the end of two years there are still traces of pus and bacilli in the urine, injections of tuberculin should be continued.

Thomson-Walker[9] states that renal tuberculosis is a disease of young adults, occurring most frequently between the ages of 20 and 40. It is rare in children, and is often bilateral in the early stages. In adults, chronic renal tuberculosis is unilateral in about 80 per cent of cases in the early stage.

Primary tuberculosis of the kidney rarely exists. A primary focus is always present elsewhere in the body, although it may not be discovered clinically. Coincident lesions were found by Braasch in 71 per cent of 346 surgical cases; they were noted by Persson in 50 per cent. In Thomson-Walker's cases, tuberculous lesions were noted elsewhere in the body in 40 per cent. In order of frequency, these extrarenal lesions are in the bones and joints and in the genital tract in the male. In Thomson-Walker's cases, there were tuberculous lesions in the epididymis in 23 per cent, in the prostate in 15 per cent and in the seminal vesicles in 7 per cent.

Miliary tuberculosis is usually an acute condition in which both kidneys are studded with tubercles. It is a part of general tuberculosis and is not of surgical interest.

Usually the first change takes place at the apex of a pyramid. Ulceration spreads outward toward the base of the pyramid, and a cavity communicating with the calix forms. Beyond this, there is a zone of inflammation which may show tubercles. Outward from this zone, isolated tubercles are scattered through the renal tissue. On the surface of the kidney, groups of tubercles are seen in areas corresponding to the subjacent tuberculous pyramids.

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9. Thomson-Walker, Sir John: Tuberculosis of the Kidney, Brit. M. J. **2**: 625, 1927.

Tuberculous lesions of the kidney may be arrested as the result of one of two processes: (1) healing of the tuberculous lesions with disappearance of the *Bacillus tuberculosis* and replacement of the ulcer with a scar, and (2) exclusion of the tuberculous focus by a ring of fibrous tissue. This may occur in three ways: tuberculous hydronephrosis, massive caseous tuberculosis of the kidney and occlusion of an ulcerocavernous focus.

The discovery of the bacillus of tuberculosis is the final proof of urinary tuberculosis. The bacillus was found in the urine in 85 per cent of Persson's cases, in 70 per cent of Beer's and in 90 per cent of Wildbolz'. In 193 cases in which Thomson-Walker performed nephrectomy for renal tuberculosis, the bacillus was found in 155 (80.3 per cent).

The modern treatment of renal tuberculosis is nephrectomy in all cases if the other kidney is healthy and there is no definite contraindication. This treatment is based on three postulates of the surgical pathology of chronic renal tuberculosis: (1) tuberculosis of the kidney is a progressive disease, (2) tuberculosis of the kidney is unilateral in the early stage and bilateral in the late stage, and (3) removal of the tuberculous kidney usually prevents infection of the other kidney.

The immediate postoperative mortality of nephrectomy in bilateral renal tuberculosis varies from 66 to 80 per cent and the benefits gained in the few surviving cases have not been permanent. The procedure is justified only in exceptional cases.

Various methods of dealing with the tuberculous ureter have been described: (1) the ureter is cut across below the kidney, the end seared with cautery or with pure carbolic acid and dropped back into the retroperitoneal space, and pure carbolic acid is injected into the ureter; (2) the ureter is cut across below the kidney and the end is sutured to the skin in the lumbar wound, or is brought up to the surface inside a drainage tube and fixed there; (3) the kidney and ureter are removed through a lumbar iliac incision (nephro-ureterectomy), and (4) the kidney is removed by the lumbar incision and the ureter cut across. A second small incision is made in the inguinal region through which the ureter is removed.

The method that Thomson-Walker uses is to remove the ureter as far as the brim of the pelvis through the lumbar wound, sear it with the cautery or with pure carbolic acid, apply a ligature, and drop it into the retroperitoneal space. The patient is reexamined in six months, and if there is reason to believe that the disease is still active in the ureter and is infecting the bladder, extraperitoneal ureterectomy is performed through a median suprapubic incision. The cases in which ureterectomy is advisable are those in which there is stricture at the lower end of the ureter and dilatation of the duct. The proportion of cases in which this is required does not exceed 8 per cent.

In most cases the wound is closed without drainage. Drainage may be necessary on account of oozing or of infection of the perinephric tissues.

The operative mortality has fallen during the last twenty-five years. Recent statistics are satisfactory. In Thomson-Walker's 193 cases the mortality was 2.5 per cent. He was able to trace 111 of 188 surviving patients; 67 were well and without symptoms of urinary disease at periods of from one to twenty-two years after the operation; 25 were in good general health but still had symptoms. Of 19 patients who died after the operation, 11 (57.8 per cent) died during the first three years.

In none of Thomson-Walker's cases was cure obtained by tuberculin. Frequently symptoms were ameliorated and the general health improved for several years, but the tuberculous disease persisted. Tuberculosis of the kidney cannot be cured by exposure of the patient to sunlight; the temporary improvement that may take place encourages the patient to refuse operation or to postpone it. Heliotherapy is valuable after the operation; it is also useful in cases in which operation is contraindicated.

In an inquiry among the physicians of Switzerland, Wildbolz found that of 316 patients suffering from renal tuberculosis and on whom operations were not performed, 31.3 per cent died within the first two years, and 27.2 per cent within from three to five years. More than half (58 per cent) died within the first five years, and only 20 per cent were alive after five years.

Fullerton [10] recently investigated a series of 158 cases of tuberculosis of the bladder that had been observed for several years. There was definite evidence of renal involvement in 141.

Fullerton's most successful operations were removal of the kidney and of as much of the ureter as could be reached through the lumbar wound. He did not find it necessary or desirable to dissect out the ureter. He believes that the removal of infected nodes surrounding the pedicle close to the spine is attended with risk. His present practice of dealing with the ureter at the point of section is to inject with a hypodermic syringe pure carbolic acid into the lumen for 2.5 cm. or more, before ligation and division of the ureter.

Nephrectomy was carried out in 73 of the cases; 6.8 per cent of the patients died as the result of operation. Fifty-five of the 68 surviving patients have been traced. Fifteen have died, 4 of them after long periods of complete relief. Forty-one patients not subjected to operation were traced; 26 (63 per cent) were dead.

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10. Fullerton, Andrew: Statistics of Post-Operative Survival in Renal Tuberculosis, Brit. M. J. **2**:630, 1927.

Statistics support the contention that, with our present knowledge, operation remains the most hopeful method of treatment. If performed early, before deep ulceration has taken place in the bladder, relief is often immediate.

[ED. NOTE.—Various reports recently have suggested the necessity of surgical procedures in unilateral renal tuberculosis. Joly [11] states that urologists are unanimous in advising early operation. Joly quotes Rafin as saying that 91 of 168 patients not operated on were dead, the majority within the first three years after the onset of symptoms. In all, about 90 per cent of patients with renal tuberculosis who are not operated on die from the disease. Even patients who survive are rarely free from symptoms. Clinical cures are so rare that they do not appreciably influence the statistics. Israel states that a nonoperative cure for renal tuberculosis does not exist. The infection may be well localized and of low virulence, or the patient may, by reason of chronicity and numerous foci of infection, have acquired a tolerance and resistance to the bacillus. Braasch believes that immunity develops with multiplicity of lesions. In most cases, the infection destroys the kidney, spreads locally, extends to the bladder, and often causes disease of the other kidney. Nephrectomy is the operation of choice. Conservative surgical procedures are not practical in cases of tuberculous kidneys, and at best afford only temporary relief.

The statistics of Kümmell [12] concerning the spread and extension of the disease noted at necropsy in cases in which operation had not been performed, suggest the course usually taken by the disease when allowed to continue without surgical interference. In a review of 40,621 necropsies from the Eppendorfer Klinik, Kümmell gives 119 cases of tuberculosis of the kidney. In 84 of the cases, the condition was bilateral and in 35, unilateral. In contrast to this, bilateral infection was found in only 5 of 100 surgical cases of renal tuberculosis.

In the cases in which operation was not performed, there was evidence of other foci of tuberculosis in 99.2 per cent and in those in which operation was performed, 44 per cent.

Pugh [13] reviews the literature and records that in 69 per cent of cases in which exacerbation of unilateral tuberculosis occurred during pregnancy, abortion or nephrectomy became necessary immediately. Thus it would seem that pregnancy, instead of increasing the necessity for conservative treatment of renal tuberculosis, would contraindicate it. As the renal process is acutely exacerbated in 71.1 per cent of the cases,

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11. Joly, J. F.: The Late Results of Renal Tuberculosis, Brit. J. Tuberc. **19**: 188, 1925.

12. Kümmell, H.: Ueber Nierentuberkulose, Ztschr. f. Urol. **17**:18, 1923.

13. Pugh, W. S.: Tuberculosis of the Kidney in Pregnancy, Ann. Surg. **86**: 591, 1927.

immediate intervention is urged. Interruption of pregnancy does not stop the tuberculous process, and this procedure is increasingly dangerous in later months.

Pugh unhesitatingly recommends nephrectomy in cases of renal tuberculosis in pregnant women. He examined the records of thirteen cases in which nephrectomy was performed by others. In eight cases, uninterrupted pregnancy and delivery at full term resulted. In four cases, abortion had to be resorted to after the nephrectomy. The diagnosis in the remaining case was vague. Of three patients observed by Pugh, two came to full term following nephrectomy. The uterus of the third was emptied at the fourth month, the patient dying one month later. Apparently pregnant women stand the operation well, and it is not more serious than when attempted in the nongravid state.

Perirenal Hematoma.—Hübner [14] states that clinical identification of perirenal hematoma was first described by Raye in 1839, and by Willis in 1841, and was called "apoplexia renum." Wunderlich later enhanced its clinical significance. There are many conjectures regarding the pathogenesis. There is no single explanation that covers all types of cases.

Perirenal bleeding does not always come from the kidney itself. Läwen describes a hemorrhage from the iliac artery, which reached from the prostate to the diaphragm and encircled the kidney. A similar observation is made by Michaux following the spontaneous rupture of the epigastric artery. Not infrequently it is impossible to determine the source of the bleeding either by operation or necropsy; in one case, a massive hemorrhage was found in the renal region following scarlet fever. True perirenal bleeding is that coming from the kidney proper or the renal capsule, as well as those cases with blood between the fibrous capsule and surface of the kidney. These are more accurately designated as "perirenal hematomas," while massive hemorrhages are designated "retroperitoneal hematomas."

Chronic renal disorders have frequently been found associated with perirenal hematoma. The condition of the walls of the blood vessel and increased blood pressure have been thought to produce a hemorrhagic diathesis. Israel designates this as essential renal bleeding because of the absence of definite symptoms. Most authors, however, favor nephritis as the causative factor.

Hübner undertook some experimental work to determine the actual cause of the bleeding. He performed nephrotomy in some instances, and in others he clamped the renal pedicle, in periods varying from ten to thirty minutes, with the idea of creating a disturbance in the renal circulation. In most instances, definite subcapsular bleeding was noted.

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14. Hübner, A.: Das Perirenale Hämatom. Experimentellar Beitrag zur Frage der Genese, Arch. f. klin. Chir. **145**:338, 1927.

It was believed that this was the result of stagnation of blood in dilated vessels and capillaries, thereby leading to bleeding by diapedesis. A series of experiments was also carried out to observe the influence of trauma, and it was concluded that the mechanism of hematoma is due to trauma and to hemorrhagic diapedesis.

Hydronephrosis.—Hellstrom [15] reports two cases of hydronephrosis in which the pelvic dilatation was probably caused by the oblique course through the wall of the pelvis of the upper end of the ureter.

Hellstrom recognizes three types of pathologic change at the ureteropelvic juncture: congenital preformations, inflammatory processes and mechanical change produced through irregular dilatations of the wall of the renal pelvis. In the two first types, therefore, the changes at the ureteropelvic juncture are the primary factors and the cause of hydronephrosis; in the third type the contrary is true. A combination of these three possibilities may occur naturally; it may then be difficult to determine which form is present. In one of Hellstrom's cases, the extrarenal portion of the renal pelvis was about 9 cm. in diameter. The ureter, which was not dilated, arose from the lower wall of the renal pelvis, curved sharply upward and was fixed for about 1 cm. to the anterior wall of the renal pelvis; from there it was unattached and turned downward in an acute angle. In the second case, the kidney was large, dilated and almost completely destroyed. The ureter started from the anterior and medial wall of the renal pelvis about 2 cm. from its lower pole and passed for a distance of about 1 cm. obliquely through the wall of the pelvis from below upward. In a third case, that of a large hydronephrotic sac, the obstruction was believed to have been caused by spastic conditions at the ureteropelvic juncture.

Herman,[16] in reporting a case of rupture of a hydronephrotic sac reviews the literature carefully. The condition is rare, from twenty-five to thirty cases only having been reported.

The case reported was that of a woman, aged 27, who was known to have pyelitis. She had been injured by a motor truck and was admitted to the hospital complaining of pain on the right side. There was tenderness and rigidity over the right flank. Signs of intra-abdominal injury were not present. The urine was bloody. A cystoscopic examination four days after the accident showed bleeding from the right kidney. A week later a pyelogram revealed rutpure of a hydronephrotic sac on the right side. Nephrectomy was followed by recovery. Only two cases are on record in which a correct preoperative diagnosis was made.

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15. Hellstrom, John: Contribution to the Knowledge of the Etiology of Hydronephrosis, Acta chir. Scandinav. **62**:167, 1927.

16. Herman, L.: Case of Ruptured Hydronephrosis, J. Urol. **18**:458, 1927.

Nephrectomy is the procedure of choice, although in certain neglected cases preliminary incision and drainage may be indicated. Molesworth advocates preliminary laparotomy, and cites three cases of concurrent peritoneal injury in support of his views; in each of these cases, however, the kidney was removed and the rent in the peritoneum closed through an incision in the loin. In the presence of symptoms strongly suggestive of intraperitoneal injury, exploratory laparotomy is indicated, but if the abdominal contents are found to be uninjured, the wound should be closed and the kidney removed through an incision in the loin.

Analysis of the small series of recorded cases justifies the statement that with the wider application of instrumental diagnostic means, exploration of the abdomen will rarely be indicated in case of rupture of the sac, since, if the true nature of the injury is recognized, one can be reasonably sure that there are no complicating intraperitoneal injuries.

Papin [17] states that in surgical treatment of hydronephrosis, two extremes should be avoided, the essentially conservative and the radical. Conservative treatment was predominant in the earlier period of renal surgical procedures, and was replaced by radical treatment. Differentiation of the cases of hydronephrosis in which surgical treatment should be given and those in which medical treatment should be administered, can be determined only by pyelography. The old surgical procedures consisted of pyeloplicature and other plastic measures on the pelvis and ureter.

Nephropexy serves satisfactorily if the ureter is kinked and is unsatisfactory in cases with small congenital dilatations. The resection of anomalous arteries, which is similar to the so-called resection of Albarran, brings about atrophy of the corresponding renal segment.

Papin resected part of the renal pelvis in 6 cases; this was followed by renal drainage and nephropexy. In 2 cases he performed partial nephrotomy with dilatation and drainage of a large superior calix; in 1 case, partial resection of the kidney was performed and in another case pyelo-ureteral anastomosis.

Ptosis.—Demel [18] reports his experience in 22 cases of nephroptosis. Operation was performed in 7 of these and there were 3 recurrences. In 1 of the 4 remaining cases a different pain developed, although the renal pain disappeared. The associated pain in 2 other definite cases of removable kidneys disappeared after appendectomy. The remaining 13 patients were not operated on. Seven of these were completely relieved by abdominal binders and 3 were greatly relieved by the wearing of supports.

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17. Papin: Les operations conservatrices dans les hydronephroses, Presse méd. **2**:1365, 1927.

18. Demel, Rudolf: Ist die Nephrophtose ein chirurgisches Leiden? Beitr. z. klin. Chir. **139**:96, 1927.

Demel states that nephropexy should not be performed: (1) in cases in which the anatomic factors are not definitely explained, (2) in cases of generalized enteroptosis, (3) in cases of painless movable kidney; (4) in cases of gastro-intestinal symptoms or (5) if patients are hysterical or neuropathic. Usually nephropexy is not a satisfactory treatment for hydronephrosis associated with movable kidney. The operation should be undertaken only in cases of marked renal pain and distention which is caused by intermittent hydronephrosis or acute obstruction due to circulatory disturbances or kinking of the renal pedicle or of the ureter.

Demel believes that the conservative nonoperative treatment should be attempted usually, and that in most cases it will be successful or partially so.

Pyelonephritis.—Stephen,[19] in discussing pyelitis in children, states that simple bacilluria may exist without cells in the urine. It is difficult to recognize bacilluria without pyuria, and often there is a long course of illness before it is correctly diagnosed. *Bacillus coli-communis* is usually the cause of pyelitis; this term covers several species besides *Bacillus coli-communis* proper, such as lactose fermenters, *Bacillus cloacae* and the *Bacillus lactis-aerogenes* and the nonlactose fermenters, *Bacillus typhosus, Bacillus proteus,* Gärtner's bacillus and Morgan's bacillus.

One hundred and eleven of the 148 patients with pyelitis who were treated at the Royal Alexandria Hospital were females. The duration of pyrexia varied from eight to sixteen days. Treatment with alkalis for long periods was usually successful. Alternating the alkalis with methenamine and sodium acid phosphate has been advised, but Stephen obtains the best results by persisting in an uninterrupted course of alkalis.

Infants, 12 months of age, frequently required and tolerate 2 Gm. (30 grains) of sodium bicarbonate and 2 Gm. potassium or sodium citrate three or four times a day. Vaccine has often proved invaluable in the treatment of chronic pyelitis in children, but usually must be continued for several weeks.

If there is a history of definite pyelitis extending over a period of months, the patient should be referred to a urologist for pelvic lavage.

Pugh [20] has studied pyelitis of pregnancy and reviews the literature carefully. He believes that urinary antiseptics are of questionable value in this disease and says that treatment should be limited to the use of large draughts of water at frequent intervals. He advises the use of the indwelling catheter as the ideal form of treatment in all cases. The

19. Stephen, E. H. M.: Pyelitis in Children, M. J. Australia **2**:142, 1927.

20. Pugh, W. S.: Pyelitis of Pregnancy; Its Treatment with Indwelling Catheter, J. Urol. **18**:553, 1927.

roentgen-ray opaque type of catheter is most satisfactory as it resists corrosion for a longer period than the ordinary plain catheter. He uses as large a catheter as possible with a large eye, cutting the meatus if necessary. The results are said to be better with the larger catheters. Pain, if it occurs from the indwelling catheter, is controlled by narcotics.

Corbus and Danforth,[21] in a study of pyelitis of pregnancy, find that although palliative and conservative measures afforded relief there was evidence of trouble persisting after delivery. In such cases treatment should be instituted after the pregnancy ends, in order, if possible, to restore adequate urinary drainage. In thirteen consecutive cases in which pyelographic studies were carried out after the termination of pregnancy, lesions were demonstrated in the urinary tract. Since lesions were present in the urinary tract after termination of pregnancy in all the cases studied, it seems reasonable to assume that they may have been present before the pregnancy began.

Crabtree [22] believes that there is a great deal that is not understood about the relationship of ureteral stricture to pyelitis of pregnancy. He is convinced that if stricture exists in many pregnant women with pyelonephritis, it is of only a few weeks' duration and that the patient recovers spontaneously after delivery. He does not think it is present in the majority of ureteral and pelvic dilatations in pregnancy. The return to normal of such kidneys without treatment for stricture is too rapid, and proper drainage measures will relieve the distention in the absence of ureteral dilatation. Crabtree recognizes that such a statement only adds to the controversy over the "clinical" stricture. In his clinic, he demonstrated in postpartem pyelonephritis an area of inflammatory change in one case sufficient to deform the course of the ureter. Stricture subsequently developed at that point. The severity of inflammatory reaction in the partially closed type of kidney found in the pregnant woman is favorable to the formation of stricture after delivery, on account of the scar tissue. In one case, a stricture developed within a year following pyelographic evidence of its absence.

The evidence available on the subject of the formation of the stricture in pyelonephritis of pregnancy is extremely meager. It is rarely possible to learn the condition of the urinary tract either before or early in pregnancy. Pyelography either during pregnancy or within three months following delivery is unreliable, since interpretations made on pyelograms taken before the kidney has recovered from the distention present during pregnancy are misleading. Different degrees of disten-

21. Corbus, B. C., and Danforth, W. C.: Pyelitis in Pregnancy, J. Urol. **18**: 543, 1927.

22. Crabtree, E. G.: Stricture Formation in Ureter Following Pyelonephritis of Pregnancy, J. Urol. **18**:575, 1927.

tion of such pelves will give entirely different pictures. The slack following distention has not yet been considered.

Pugh has found that the stricture occurs in the ureter at points where there can be no pressure from the fetus; it is the result of inflammatory changes attendant on pyelonephritis of pregnancy. It is noteworthy that the few strictures which have been observed in the pregnant women of his clinic did not cause symptoms immediately after delivery but months afterward.

Eisendrath [23] makes a plea for the more widespread use of the inlying ureteral catheter in the treatment of persons with pyelonephritis and other renal conditions. Ordinarily, in lavage of the renal pelvis, the ureteral catheter is withdrawn immediately.

The inlying catheter, first recommended for the relief of obstructive aneuria and nontuberculous renal infections, now is used: (1) for the relief of aneuria of the obstructive type, (2) in the treatment of patients with acute and chronic pyelonephritis, (3) for relief from pain resulting from ureteral obstruction, (4) in cases of ureteral injury following pelvic operations, and (5) as a method of drainage of the kidney after the repair of a vesicovaginal fistula.

Eisendrath employs small roentgen-ray ureteral catheters, as the coating is more durable on the opaque than it is on the nonopaque catheter. Only a single catheter is inserted into the ureter of the affected side. Irrigation of the renal pelvis is not necessary, as there is ample drainage through the lumen or alongside the inlying catheter. The time the catheters can be left in place varies. If they tend to be expelled, a small urethral catheter can be introduced into the bladder to avoid accumulation of urine.

Crosbie, in discussing Eisendrath's paper, states that he believes drainage should be reserved for cases of obstruction, in which the pelvis of the kidney cannot drain itself. A ureteral catheter cannot be left in long without causing a certain amount of injury to the ureter.

Merritt states that he had found the failure to irrigate the renal pelvis to be the cause of catheter blockage in many cases, and for this reason he now uses two catheters irrigating with sterile water and then a solution of mercurochrome-220 soluble through one.

Livermore maintains that stasis is the chief cause of infections of the kidney. Although there may be a definite focus of infection, it does not lodge in the kidney unless stasis is present or the dosage overwhelming. If there is obstruction, the kidney will unquestionably be infected.

Bumpus states that another type of case which has not been mentioned in the treatment with the inlying catheter is pyelitis of pregnancy.

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23. Eisendrath, D. N.: Inlying Ureteral Catheter in Treatment of Pyelonephritis and Other Renal Conditions, J. A. M. A. **89**:2170 (Dec. 24) 1927.

He believes that if the patient is ill, drainage should be instituted, and the indwelling ureteral catheter gives the best results. In studying a large series of pyelograms, he has seen dilated calices and pelves which have made him consider the possibility of previous pyelonephritis, but the history did not confirm this; on further investigation, however, he has found this to be the result of previous pregnancies.

Kretschmer does not agree with Eisendrath as to the advisability of routine drainage in cases of acute pyelonephritis by means of the indwelling ureteral catheter. He does not use drainage in those cases except in pregnancy, and then not often.

Hooe states that he left the catheter in one side for eight days and in the other side fourteen days. Untoward results did not follow.

Pyelovenous Back-Flow.—Gile [24] reports a comprehensive group of experiments which he recently carried out in the hope of determining the mechanism of pyelovenous back-flow. In corrosion specimens of the renal pelvis of cadaveric specimens, venous outbranchings were not obtained except when extravasation had occurred.

The results from injections of dye were similar to those of Hinman; the venous system was injected regularly, the tubules were never more than partially injected and this rarely. Roentgen-ray observations of opaque solutions injected confirmed those made by Hinman. None of these observations, however, demonstrate how the substances reach the blood stream from the pelvis. Normally, there is no intrapelvic pressure. Under a positive pressure, there may be microscopic ruptures, filtration, osmosis, increased permeability of the pelvic membrane, lymphatic absorption or the opening up of a direct communication already present in the angles of the minor calices as suggested by Hinman.

The tubules are undoubtedly partially injected, but since dye is found in the blood vessels and not in the tubules following injection of living mammalian kidneys, it would seem that they are not significant in the production of back-flow.

The living kidney of the frog apparently presents a different mechanism, as in it the tubules were easily filled.

The term "pyelovenous back-flow" is illustrative, if it is understood in a general sense, of the passage of substances from the renal pelvis to the venous circulation. Probably this phenomenon does not occur by way of the tubules; its exact route has not yet been demonstrated.

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24. Gile, H. H.: Observations on Injections of the Renal Pelvis, J. Urol. **18**:621, 1927.

(To be continued)

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